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THE UNIVERSITY OF ALBERTA

SOME SYNTHETIC ASPECTS OF ORGANOCOPPER,  
-ALUMINUM, AND -BORON REAGENTS

by



ROBERT BASIL LAYTON

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES AND RESEARCH  
IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE

OF

DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY

EDMONTON, ALBERTA

SPRING, 1972



38A

THE UNIVERSITY OF ALBERTA  
FACULTY OF GRADUATE STUDIES AND RESEARCH

The undersigned certify that they have read, and  
recommend to the Faculty of Graduate Studies and  
Research for acceptance, a thesis entitled

"SOME SYNTHETIC ASPECTS OF ORGANOCOPPER, -ALUMINUM  
AND -BORON REAGENTS"

submitted by ROBERT BASIL LAYTON in partial fulfil-  
ment of the requirements for the degree of Doctor  
of Philosophy.



TO MARY AND STEFANIE



A B S T R A C T

A new synthesis of  $\gamma,\delta$ -unsaturated ketones was achieved, based on the reaction of  $\alpha,\beta$ -unsaturated ketones with a vinylcuprate complex. This reagent appeared to offer an advantage over other methods of accomplishing conjugate vinyl addition in certain structurally hindered situations.

Diethylalkynylalanes (easily prepared by the reaction of diethylaluminum chloride with a lithium acetyl-ide) were found to efficiently transfer an alkynyl group to the  $\beta$ -carbon of a variety of conjugated enones. Varying amounts of the 1,2-addition product were also formed. Cyclic enones (such as cyclohexenone and isophorone) underwent 1,2-addition exclusively. The utility of this new method for further transformation into cyclopent-enones was briefly investigated.

The reaction of dialkylalkenylalanes with  $\alpha,\beta$ -unsaturated ketones was also examined. Although the vinyl moiety was transferred to the  $\beta$ -carbon of the enone, yields of the conjugate adduct were lower than those of the dialkylalkynylalane with the corresponding enone.

Several trialkynylboranes were prepared and found to react efficiently with ethyl diazoacetate to give propargylic esters in good yield. The propargylic esters were found to hydrate regioselectively to give good



yields of  $\gamma$ -keto esters.

The reaction of a dihaloarylborane with a diazo-ester and a diazoketone was attempted. The reaction proceeded to give the desired aryl ester in quantitative yield. A lower yield was realized with the diazoketone reaction.



A C K N O W L E D G E M E N T S

The author wishes to thank Mr. R. Swindlehurst and his staff and Messrs G. Bigam, D. Gifford and T. Brisbane for recording the infrared and nmr spectra, Dr. A. Hogg and staff for running the mass spectra and Mrs. D. Mahlow and Mrs. A. Dunn for determining the microanalyses. Thanks are also due to Mrs. M. Waters for the typing.

The author is indebted to the National Research Council of Canada for the awarding of a 1967 (Centennial) Science Scholarship to enable this work to be accomplished.

Finally, the author wishes to express his sincere thanks to his research director, Dr. J. Hooz, for encouragement and invaluable assistance during the course of this work and the writing of this thesis.



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REACTION OF CONJUGATED ENONES WITH DIVINYLCOPPERLITHIUM

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TRI-*n*-BUTYLPHOSPHINE COMPLEX. A NEW PREPARATION OF  $\gamma,\delta$ -

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UNSATURATED KETONES

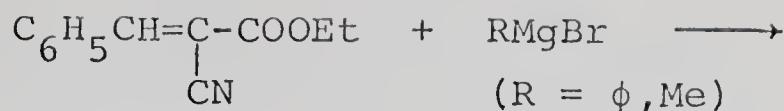
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INTRODUCTION

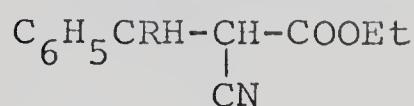
The presence of a conjugated system in a variety of  $\alpha,\beta$ -unsaturated esters, ketones, and aldehydes offers the possibility of not only the 1,2- or normal carbonyl addition, but also the 1,4- or conjugate addition of an organometallic reagent. In spite of the fact that it appears that both 1,2- and 1,4-addition occur simultaneously, many systems have been demonstrated to preferentially undergo conjugate addition.

Kohler<sup>1,2,3</sup> has shown that phenylmagnesium bromide prefers to add 1,4- to completely conjugated aryl ketones such as benzalacetophenone. He has also demonstrated<sup>4</sup> that ethyl  $\alpha$ -cyanocinnamate (I) prefers to add Grignard reagents in a conjugate manner. Normant<sup>5</sup> has found that cross-conjugated esters, nitriles, and ketones (II a, b, and c) add vinyl Grignard reagents conjugately in good yields to produce the corresponding  $\gamma$ -ethylenic derivatives. These same systems can also add an acetylenic moiety in a conjugate sense.

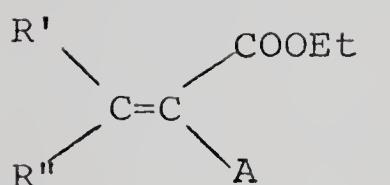




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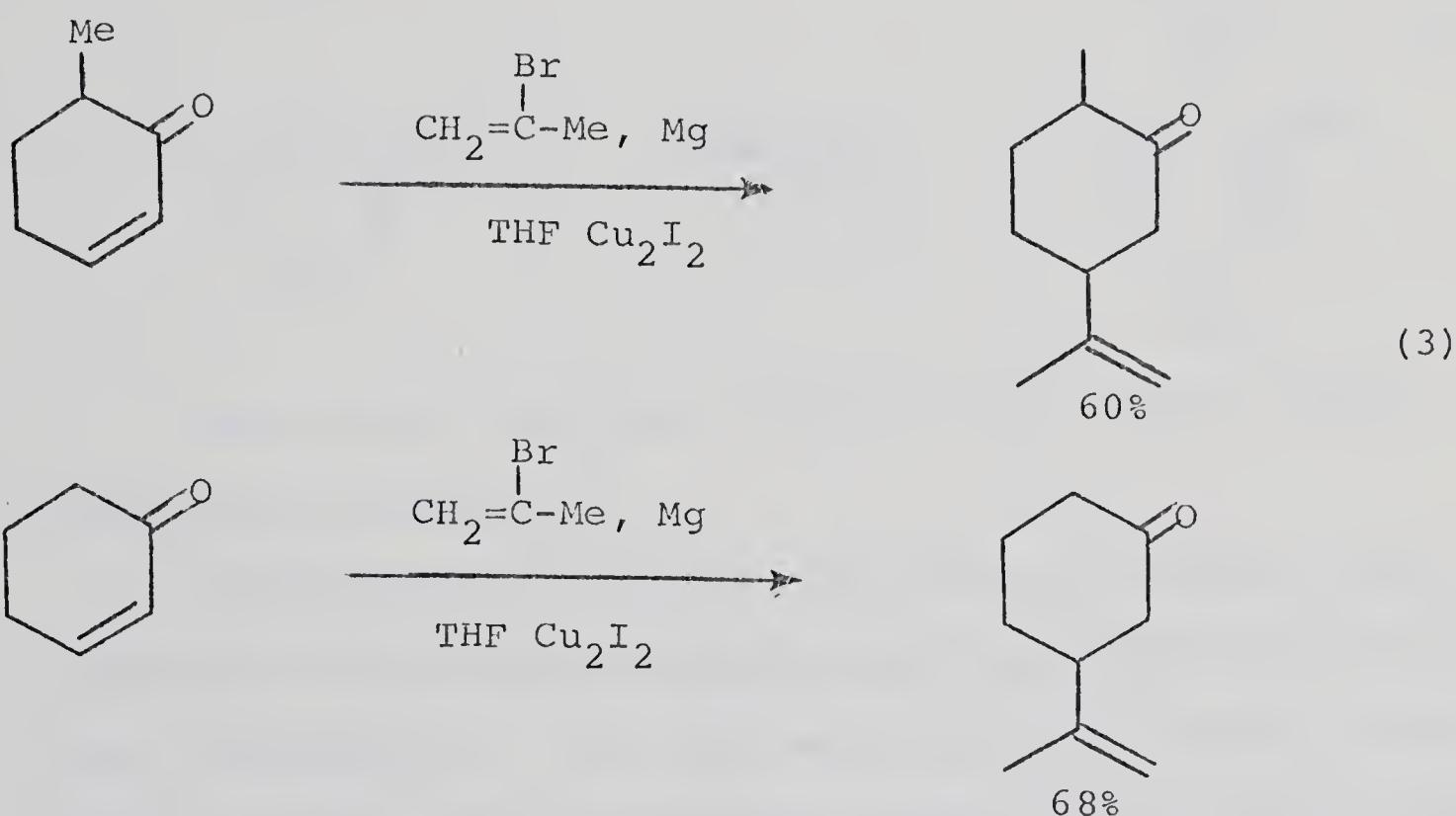
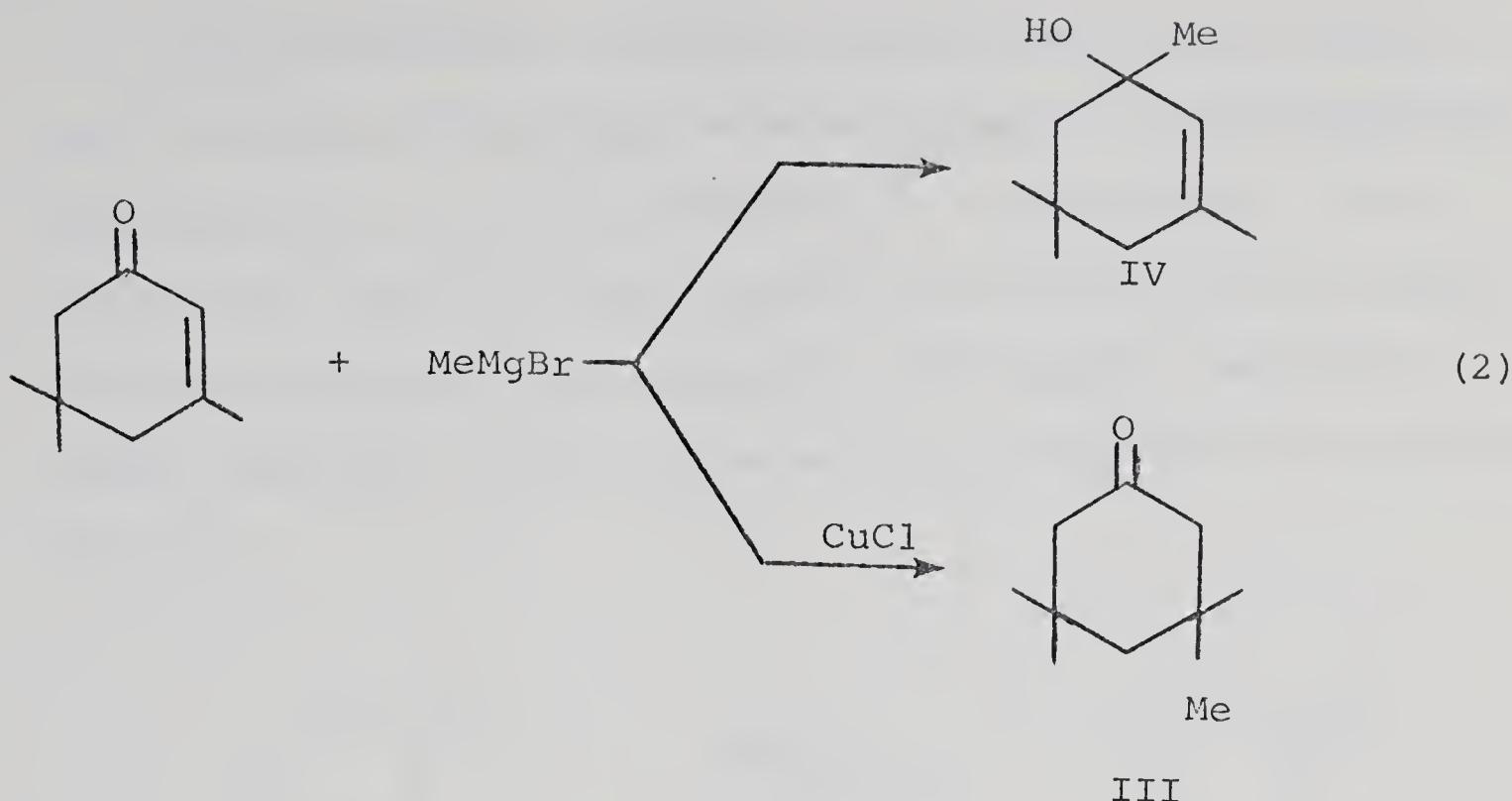
II a, A  $\equiv$  COOEtb, A  $\equiv$  CNc, A  $\equiv$  COCH<sub>3</sub>

Until recently, however, the system with by far the most general applicability to achieving conjugate addition employed catalytic amounts of copper salts in the reaction of Grignard reagents with  $\alpha,\beta$ -unsaturated carbonyl species.

Kharasch<sup>6</sup> found that addition of as little as one mole percent of cuprous chloride to the reaction of methylmagnesium bromide with isophorone produces the conjugate adduct III in 83% yield. A complete reversal resulted when no catalyst was present and a 91% yield of 1,2-addition product, IV, was obtained (eq. 2).

Vinylic Grignard reagents have also been employed with copper salt catalysis<sup>7,8</sup> to efficiently transfer an  $\text{sp}^2$ -hybridized carbon atom to the  $\beta$ -carbon of certain enones (eq. 3).

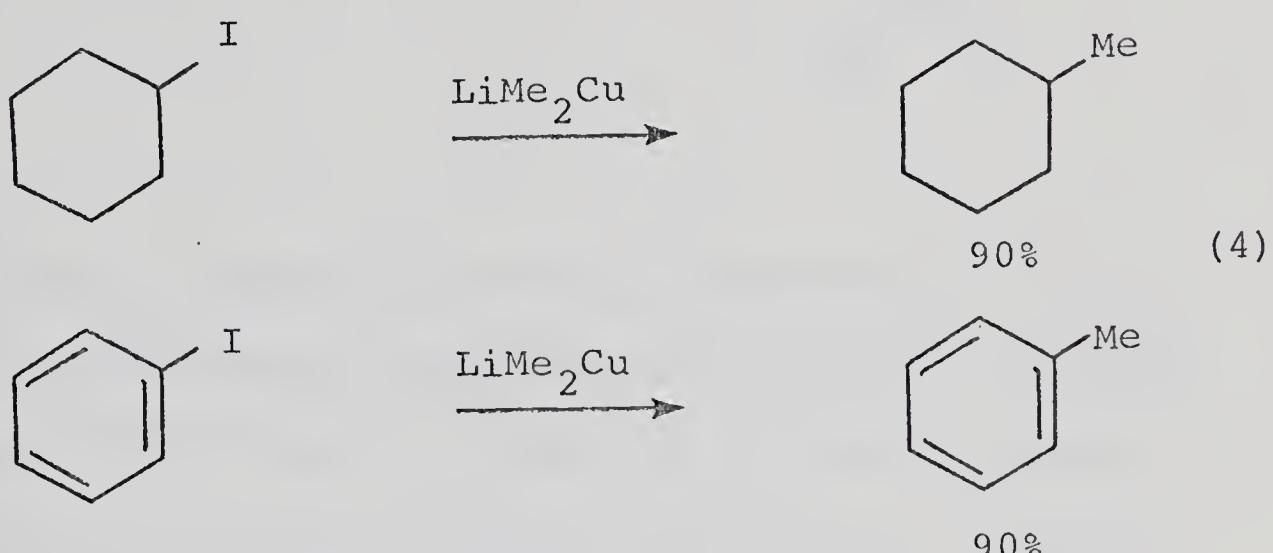




Attempts<sup>9,10</sup> at achieving the conjugate addition of an acetylenic moiety, however, have to date been uniformly unsuccessful.

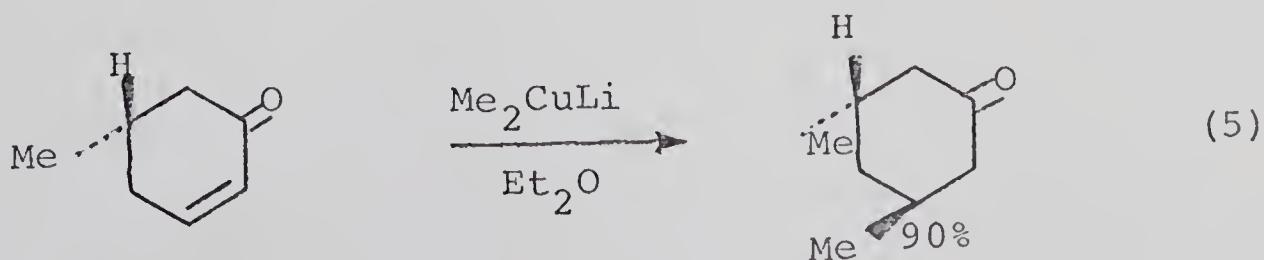


The discovery of lithium dimethylcuprate by Gilman and co-workers<sup>11</sup> sparked renewed interest in the properties and reactions of "ate" complexes.<sup>12</sup> Alkylcuprates have since been used in a wide variety of reactions with considerable synthetic value. Corey<sup>13</sup>, for example, employed these compounds to perform selective cross-coupling reactions (eq. 4).



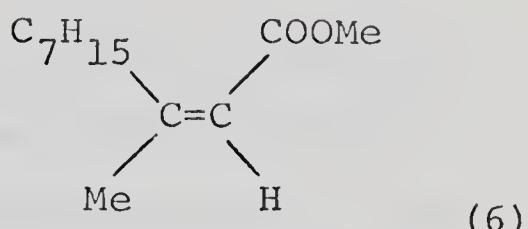
This method has been studied in much greater detail by House and co-workers.<sup>14</sup>

Organocuprates have also been shown to possess great potential for conjugate addition with  $\alpha,\beta$ -unsaturated carbonyl derivatives. Thus with enone systems, dialkyl- and diarylcuprates afford excellent yields of the ketone arising from conjugate addition of the alkyl or aryl moiety<sup>15</sup> (eq. 5).

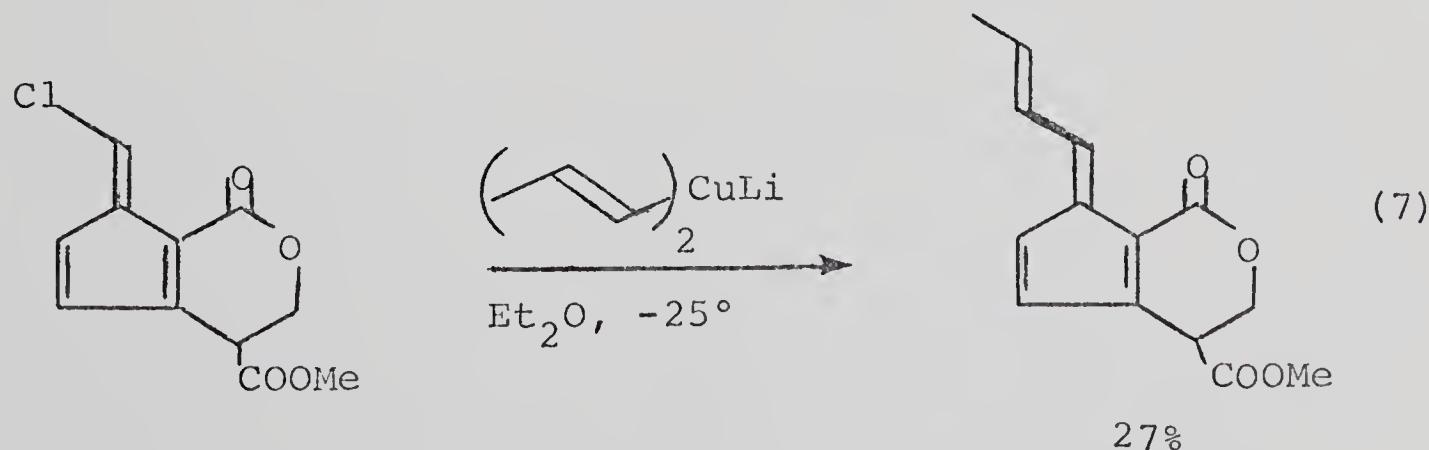




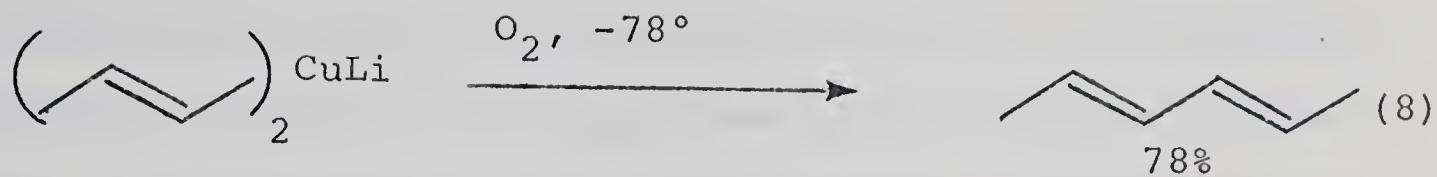
With  $\alpha,\beta$ -acetylenic esters<sup>16a,b</sup>, tri- and tetra- substituted  $\alpha,\beta$ -ethylenic esters have been obtained stereospecifically (eq. 6).



Dialkenyl cuprates have been synthesized and demonstrated to efficiently participate in the cross coupling reactions<sup>14,17,18</sup> (eq. 7) as well as to provide dienes via oxidatively or thermally induced dimerization<sup>19</sup> (eq. 8).







The purpose of the present work was to investigate the reaction of an alkenylcuprate (namely divinylcopper-lithium) with a series of  $\alpha,\beta$ -unsaturated ketones in the hope of achieving the conjugate addition of the  $\text{sp}^2$ -hybridized moiety. During the course of the investigation it was found that this method appears to offer definite advantage over previously mentioned reagents in certain structural situations.



## R E S U L T S    A N D    D I S C U S S I O N

The observations of House and co-workers that dimethylcopperlithium afforded excellent yields of the conjugate addition product<sup>15</sup> with  $\alpha,\beta$ -unsaturated ketones coupled with Corey's report of excellent yields in the conjugate addition of dialkylcopperlithium reagents to  $\alpha,\beta$ -acetylenic esters<sup>16a</sup> indicated that a dialkenylcopperlithium species might hold promise for the addition of an  $sp^2$ -hybridized moiety to the  $\beta$ -carbon of an enone system.

Divinylcopperlithium species have been synthesized by the addition of two mole equivalents of a solution of an alkenyllithium salt in tetrahydrofuran (THF) to either a slurry of one mole equivalent of cuprous iodide in THF at -78°, or, alternatively, to a solution of one mole equivalent of tetrakis[iodo-(tri-*n*-butylphosphine)copper(I)]<sup>20</sup> dissolved in THF at -78°. The latter method has the disadvantage of contaminating the crude product mixture with large amounts of tri-*n*-butylphosphine and its reaction products and hence complicating the isolation of the desired product. However, in the course of this study it was found that this shortcoming was more than outweighed by the increase in the rate of reaction of the phosphine-stabilized cuprate over that of the non-stabilized organometallic.

For the first attempt at reaction of a vinylcuprate with an  $\alpha,\beta$ -unsaturated ketone a 5:1 ratio of a non-stabilized



divinylcopperlithium species to enone substrate was chosen. Corey<sup>13</sup>, Vig<sup>18</sup> and Büchi<sup>17</sup> have employed 5:1 ratios of cuprate to alkyl halide in their investigations of the cross-coupling reaction. House, however, used ratios ranging from 1:1 to approximately 2:1 of organo-copper reagent to enone to effect conjugate addition.<sup>15</sup>

In an exploratory run the phosphine free divinyl-copperlithium was prepared by reacting two mole equivalents of an ethereal solution of vinyl lithium with one mole equivalent of a suspension of purified<sup>20</sup> cuprous iodide in ether at -78°. The resultant greenish solution, on treatment with 0.2 mole equivalent of benzalacetophenone in ether at -78°, gave a deep purple heterogeneous mixture. Upon warming to -30° the solution became homogeneous, and after being stirred at this temperature for ~16 hrs it was quenched by pouring into saturated ammonium chloride solution. Workup and chromatography afforded the crude conjugate addition product in 65% yield.

This result indicated the feasibility of using vinyl-cuprates to effect conjugate addition to an enone system.

The above reaction was repeated using only a 2:1 ratio of cuprate to enone and also employing a phosphine-stabilized cuprate. Tetrahydrofuran was substituted for ether as the solvent. The reagent was easily prepared by the addition of two mole equivalents of a solution of vinyl lithium in THF



to one mole equivalent of tetrakis[iodo(*tri-n*-butylphosphine)copper(I)]<sup>20</sup> dissolved in THF at -78°. One half mole equivalent of benzalacetophenone was then added and the mixture was stirred at -78° for 0.5 hr. Hydrolysis of an aliquot of the reaction mixture at this time and examination by infrared spectroscopy showed that the carbonyl absorption had shifted completely from 1670 cm<sup>-1</sup> ( $\alpha,\beta$ -ethylenic carbonyl) to 1690 cm<sup>-1</sup>, indicating deconjugation of the carbonyl group. The reaction mixture was quenched by pouring into saturated NH<sub>4</sub>Cl. Careful chromatography on alumina (Activity III) allowed separation of the desired product from the bulk of the phosphine in 89% yield.

The shorter reaction time of this experiment relative to the first emphasizes the advantageous rate increase gained by the use of a phosphine-complexed cuprate over an uncomplexed cuprate. This conclusion was given further credence when the reaction of the vinylcuprate with 1-acetylcylohexene was examined.

Reaction of two mole equivalents of unstabilized cuprate with one mole equivalent of 1-acetylcylohexene at -30° in THF overnight resulted in greater than 30% of the starting enone remaining unreacted. However, if the same ratio of phosphine-stabilized cuprate to enone substrate was allowed to react for only 0.5 hr at -78° the acetyl-cyclohexene was completely consumed (by ir) and a 70% yield of the vinyl conjugate addition product was obtained.



As a direct consequence of these results it was decided to survey the reaction of the phosphine-stabilized vinylcuprate with a variety of enones of different structural types to assess its applicability to the synthesis of  $\gamma,\delta$ -unsaturated ketones. The results of this survey will be found in Table I. The results of the uncomplexed cuprate reactions have been included at the end of the Table for comparison purposes.

The  $\gamma,\delta$ -vinyl ketones were very prone to polymerization and care had to be exercised in devising workup conditions which would prevent this polymerization. Hence the reaction mixtures were quenched with saturated ammonium chloride solution and the subsequent chromatography on silicic acid or alumina was conducted as rapidly as possible.

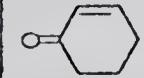
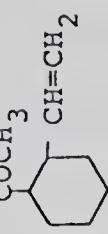
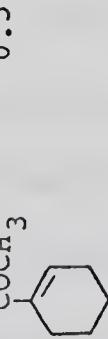
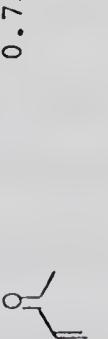
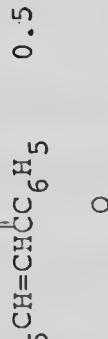
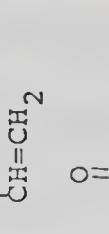
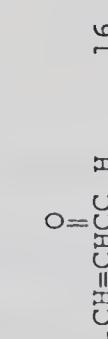
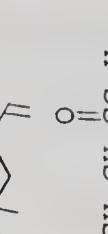
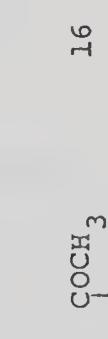
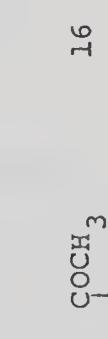
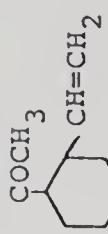
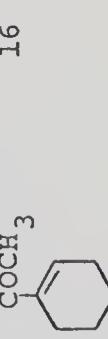
A brief comparison was made between the efficiency of the vinylcuprate conjugate addition and that of the copper-catalysed vinyl Grignard addition. The reaction of vinylmagnesium bromide with cyclohexenone in the presence of 5 mole percent cuprous iodide gave a 69% yield of 3-vinylcyclohexanone. This compares favourably with the 65% yield obtained with divinylcopperlithium and the same enone.

House<sup>7</sup> and Vig<sup>8</sup> have shown that copper-catalysed addition of isopropenyl Grignard reagent to 2-cyclohexen-1-one and 6-methyl-2-cyclohexen-1-one afford the conjugate adducts in 68% and 60%, respectively. However, there are no examples in the literature of the addition of a vinyl moiety to  $\beta,\beta$ -



TABLE I

The Reaction of Divinylcopperlithium Species with  $\alpha,\beta$ -unsaturated Ketones

Cuprate	$\alpha,\beta$ -unsaturated ketone	Reaction time (hr)	Ratio cuprate:enone	Temperature ( $^{\circ}\text{C}$ )	Enone Remaining %	Product	Yield 1,4 Product (%)
$(\text{CH}_2\text{CH})_2\text{CuLiP}(\text{nBu})_3$		0.5	2:1	-78	0		65
$(\text{CH}_2\text{CH})_2\text{CuLiP}(\text{nBu})_3$		0.5	2:1	-78	0		70
$(\text{CH}_2\text{CH})_2\text{CuLiP}(\text{nBu})_3$		0.75	2:1	-78	0		70
$(\text{CH}_2\text{CH})_2\text{CuLiP}(\text{nBu})_3$		0.5	2:1	-78	0		89
$(\text{CH}_2\text{CH})_2\text{CuLiP}(\text{nBu})_3$		2.0	2:1	0	0		72
$(\text{CH}_2\text{CH})_2\text{CuLiP}(\text{nBu})_3$		1.0	2:1	0	0		85
$(\text{CH}_2\text{CH})_2\text{CuLi}$		16	5:1	-30	8		65
$(\text{CH}_2\text{CH})_2\text{CuLi}$		2:1	2:1	-30	30		~30



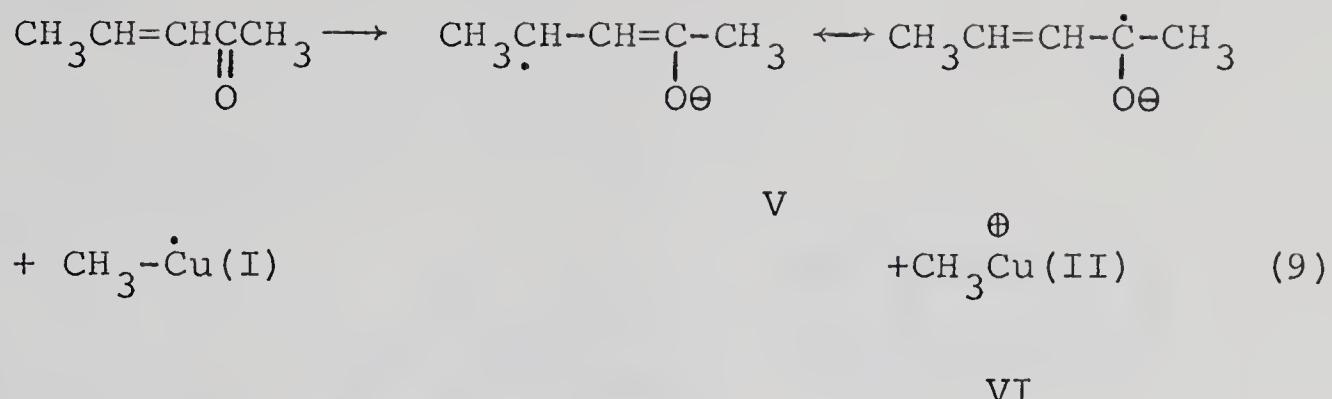
disubstituted (and hence more sterically hindered) enone systems such as mesityl oxide or isophorone.

Consequently the reaction between vinylmagnesium bromide and both isophorone and mesityl oxide in the presence of five mole percent of cuprous iodide catalyst was investigated. The isophorone reaction yielded only eight percent of the conjugate adduct while with mesityl oxide a seven percent yield of the conjugate addition product was obtained. When these results are compared with the yields of the corresponding products using the vinylcuprate reagent (i.e. 85% and 72% respectively) it becomes evident that the cuprate must be the reagent of choice for conjugate addition with  $\beta,\beta$ -disubstituted enones. These results also indicate that different intermediates must be involved in the catalysed Grignard reaction and the vinylcuprate reaction.

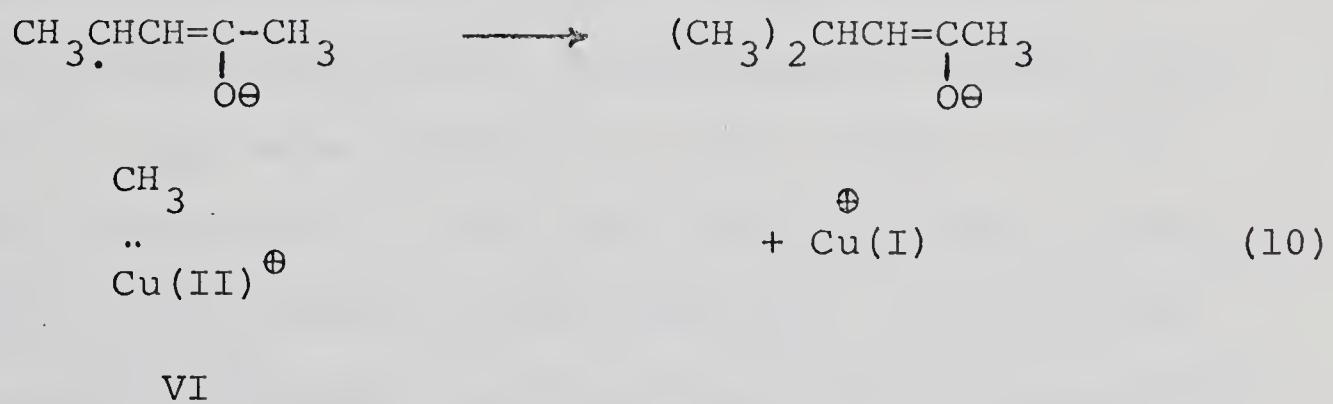
Although the mechanistic details of both the copper-catalysed Grignard reaction and the reaction of organo-cuprates with  $\alpha,\beta$ -unsaturated ketones are not fully understood, recent work <sup>15</sup> has discounted the intermediacy of free radicals, carbanions, or a pathway involving a cyclic six-centered transition state. House <sup>15</sup> has hypothesized that either partial or complete electron-transfer from organometallic to enone takes place to give rise to, respectively, either a charge-transfer complex, or an



ion radical (V).

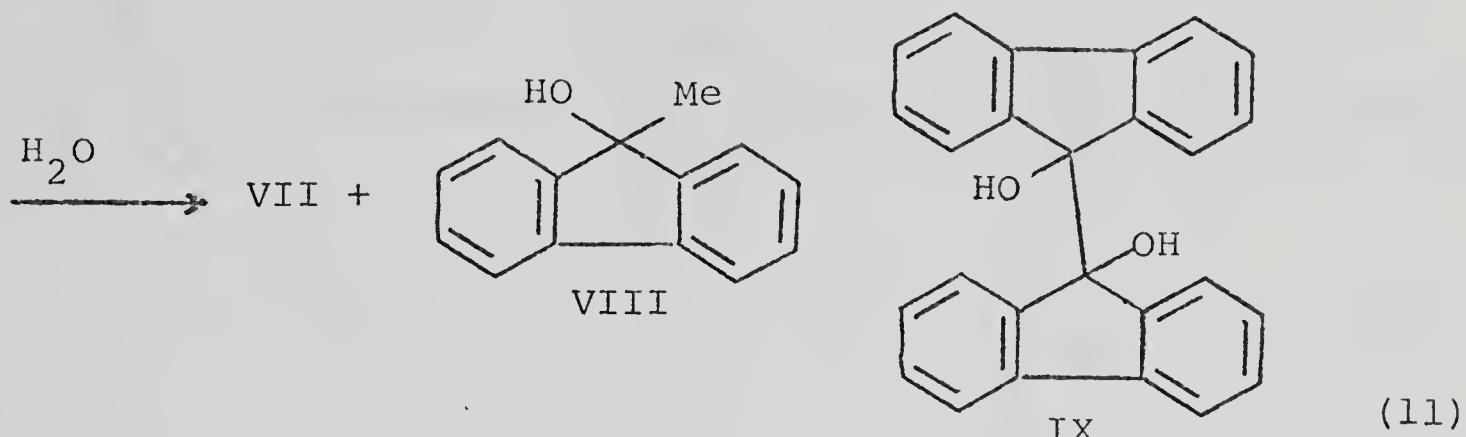


Subsequent transfer of a methyl radical from a transient methylcopper(II) species (VI) or collapse of the charge-transfer complex would complete the addition sequence.

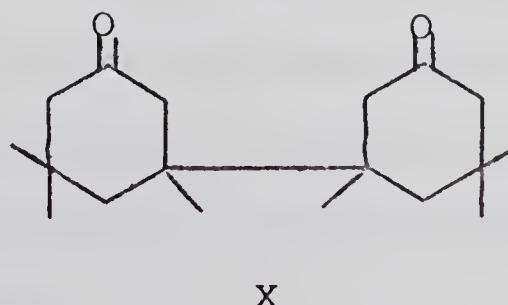


Some evidence favouring this idea was found by House in the reaction of lithium dimethylcopper with fluorenone-(VII). Hydrolysis of the green solution obtained from fluorenone and lithium dimethylcopper(I) afforded a mixture of fluorenone (VII) and the alcohols VIII and IX.



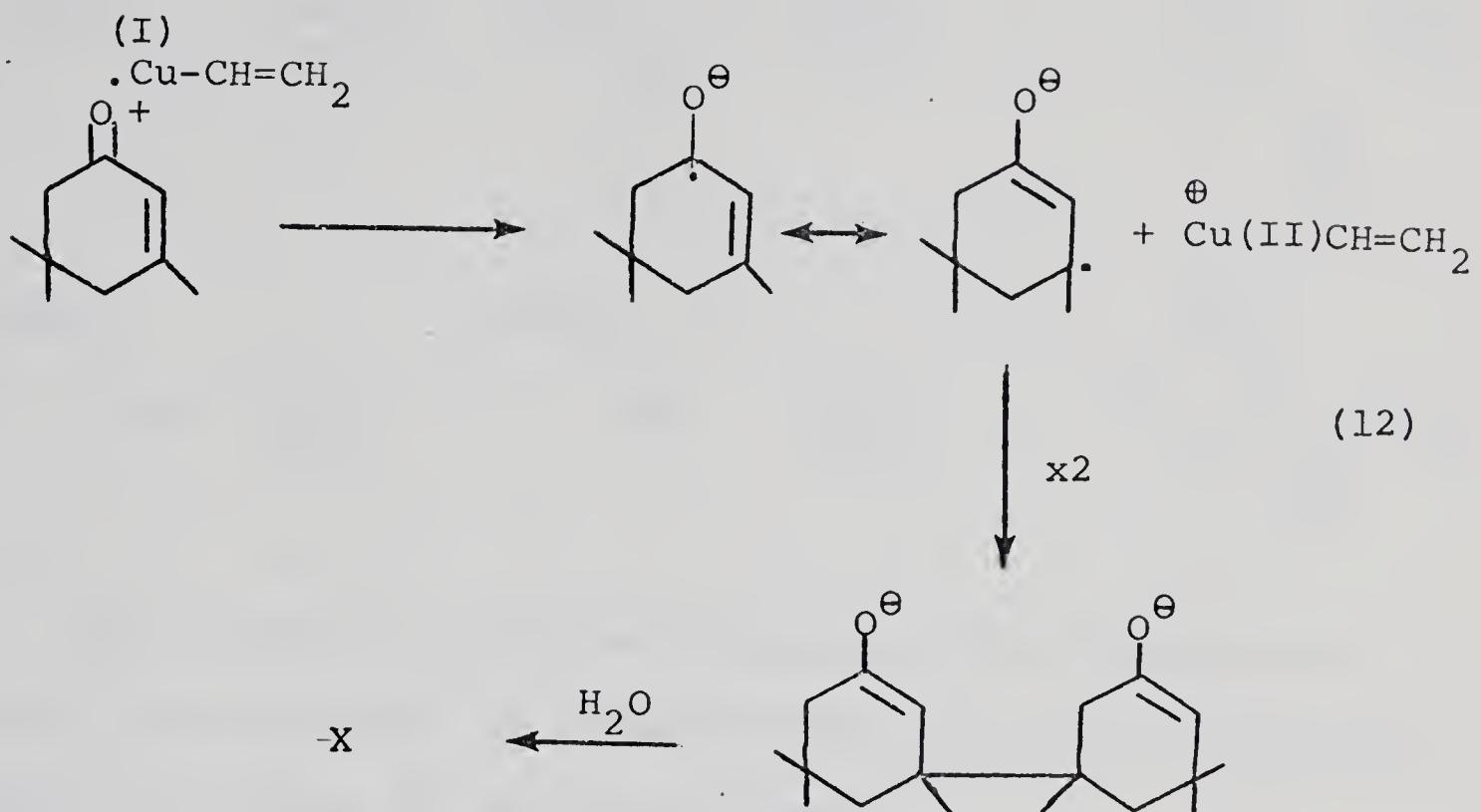


An observation made in this study concerning the copper-catalysed reaction of vinylmagnesium bromide with isophorone lends some credence to the validity of this mechanism as applied to Grignard reactions. Approximately 7% of dimer X was isolated after hydrolysis of the blue-black solution obtained from isophorone and vinylmagnesium bromide-cuprous iodide.



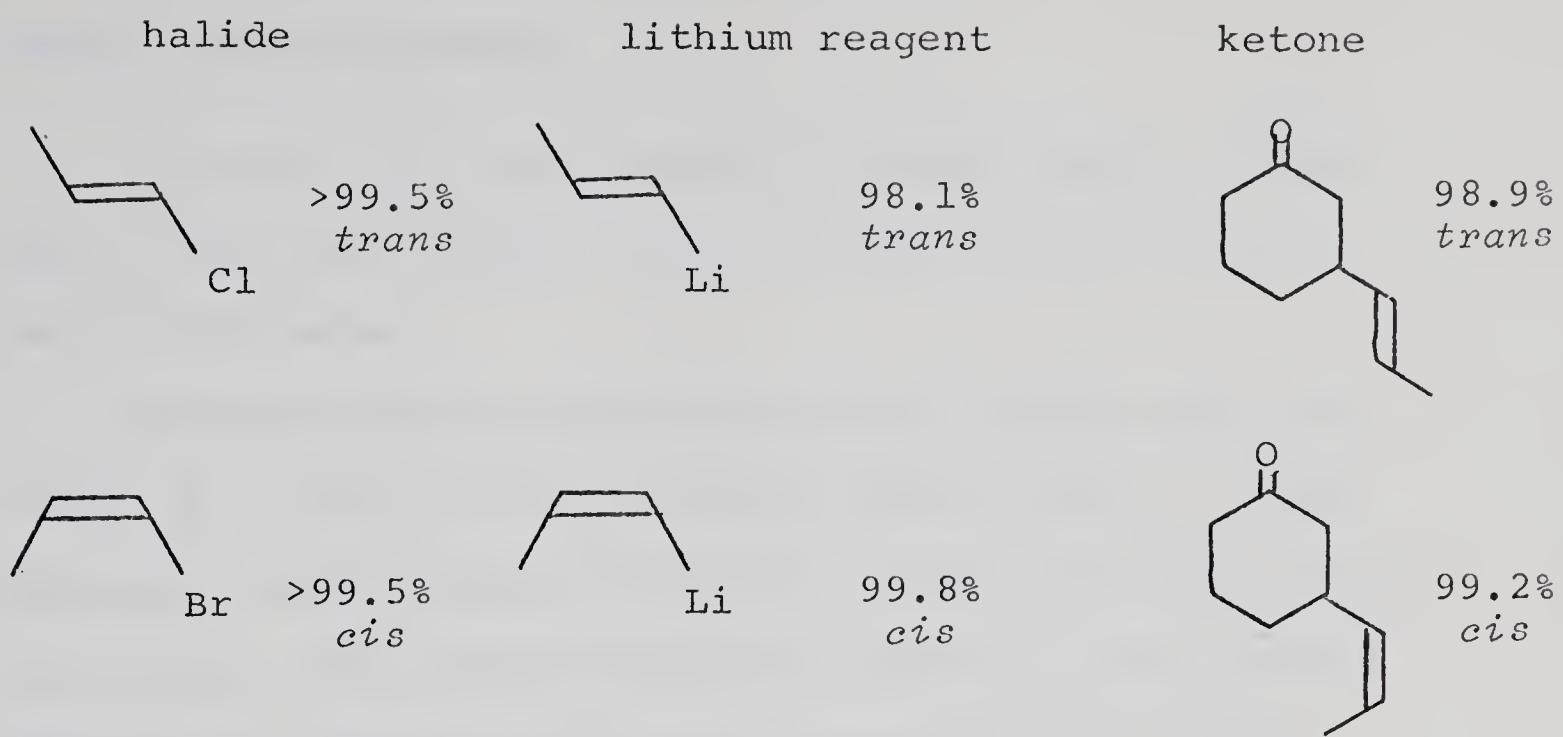


This product could have resulted from a process analogous to that proposed by House in equation 10.



Subsequent to the work done in this thesis Casey and Boggs<sup>25</sup> have reported a study of the addition of isomeric lithium dialkenylcuprates to cyclohex-2-en-1-one. They found that the stereochemistry of the starting vinyl group is retained in the product. Thus the *trans*-1-propenyl-lithium gives rise to *di-trans*-1-propenylcuprate which adds to cyclohexenone to give 3-*trans*-(1-propenyl)cyclohexanone. Similar stereospecific results were observed in the case of the *cis* olefin:





As a result, the stereochemistry of the double bond in the 1,4 adduct can be determined by the choice of lithium reagent in making the dialkenylcuprate.



E X P E R I M E N T A LGeneral Considerations.

Infrared (ir) spectra were recorded using a Perkin-Elmer 337G, Perkin-Elmer 471G or Unicam SP1000 Infrared Spectrophotometer.

Nuclear magnetic resonance (nmr) spectra were recorded on a Varian A-60 or HR-100 Spectrometer. Unless otherwise stated deuteriochloroform ( $\text{CDCl}_3$ ) was employed as the solvent with tetramethylsilane (TMS) as the internal reference. Chemical shifts are reported as  $\tau$  values relative to TMS = 10. The following abbreviations are used in the text: s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet.

Mass spectra were recorded on an AEI Model MS-2 or Model MS-9 Spectrometer.

Gas-liquid chromatography (glc) was performed using an Aerograph A-90-P3 and a Varian Aerograph Series 1200 gas chromatograph.

Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected.

Refractive indices were measured on a Bausch and Lomb Abbé-3L Refractometer.

Preparation of an Ethereal Solution of Vinyllithium.

Ethereal vinyllithium was prepared by removing the



solvent from a commercially available<sup>21</sup> THF solution of vinyl lithium *in vacuo* and adding dry ether to the solid residue. After filtration under nitrogen, the slightly yellow solution was standardized by the double titration method of Gilman.<sup>22</sup>

Reaction of Benzalacetophenone with Divinylcopperlithium.

Purified cuprous iodide<sup>20</sup> (6.13 g; 36 mmole) was suspended in dry ether (25 ml) at -78° and an ethereal solution of vinyl lithium (72 mmole) was added slowly, keeping the temperature below -50°. Upon completion of the addition, a deep green solution resulted. This was stirred for one hour at -78°, and then benzalacetophenone (1.44 g; 7 mmole) in ether (50 ml) was slowly added (1 hr). The resulting purple heterogeneous mixture was warmed to -28°, stirred overnight at this temperature and then quenched by pouring into saturated NH<sub>4</sub>Cl solution (exothermic). The organic layer was separated and the aqueous phase was extracted with ether (3 x 50 ml). The combined organic phase was dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated. The yellow residue was chromatographed over neutral (Woelm) alumina (Activity IV) using benzene:chloroform (1:1 by volume) as eluant. 3,5-Diphenyl-1-penten-5-one was obtained as a slightly yellow oil in 65% yield. Molecular distillation at reduced pressure afforded a water-white oil



which crystallized on cooling to 5°C, ir (CHCl<sub>3</sub>) 1680 (C=O), 3080, 1633, 915 cm<sup>-1</sup> (H<sub>2</sub>C=CH-); nmr: τ 2.0-3.0 (m,10) Ar, 3.69-4.35 (m,1) CH<sub>2</sub>=CH-, 4.90 (s,1) HCH=CH-; 5.15 (broad d, 1) HCH=CH-, 5.909 (m,1) CH-CH<sub>2</sub>-; 6.62 (d,2) CH-CH<sub>2</sub>; mass spectrum m/e (calc. for C<sub>17</sub>H<sub>16</sub>O 236.1201. Found 236.1202): 236(6), 221(5), 117(12), 115(11), 106(10), 105(100), 91(9), 77(25), 51(8). No satisfactory elemental analysis could be obtained for this compound.

#### Tetrakis[iodo-(tri-*n*-butylphosphine)copper(I)]

A decolourized solution of cuprous iodide (39.45 g; 200 mmole) in saturated aqueous potassium iodide was treated with freshly distilled tri-*n*-butylphosphine (37.5 ml, 30.2 g; 150 mmole) as described by Kauffman *et al.*<sup>20</sup> The white crystalline product was filtered and recrystallized from ethanol:isopropanol (1.5:1 by volume) to afford tetrakis-[iodo-(tri-*n*-butylphosphine)copper(I)] as long, colourless needles, m.p. 74.5-75° (lit.<sup>20</sup> 75°) in 50% yield.

#### Reaction of Benzalacetophenone with Tri-*n*-butylphosphine-stabilized Divinylcopperlithium.

Tetrakis[iodo-(tri-*n*-butylphosphine)copper(I)] (7.52 g; 20 mmole) in THF (20 ml) was treated with a solution of vinyl lithium in THF (40 mmole) at -78°C. Benzalacetophenone (2.0 g; 10 mmole) dissolved in THF (20 ml) was added to the resultant blue-black solution over 20 minutes, keeping the temperature below -50°. The solution was then stirred at -78° for 15 minutes and an aliquot was removed and hydrolysed



with saturated  $\text{NH}_4\text{Cl}$ . An infrared of the dried organic layer showed a complete shift of carbonyl absorption from 1670 to 1690  $\text{cm}^{-1}$ . The bulk of the reaction mixture was quenched by pouring into saturated  $\text{NH}_4\text{Cl}$ . The aqueous phase was extracted with ether ( $3 \times 50$  ml) and the combined organic phase was dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated. The yellow residue was chromatographed over neutral (Woelm) alumina (activity III) using benzene:chloroform (1:1 by volume) as eluant. 3,5-Diphenyl-1-penten-5-one was obtained as a slightly yellow oil in 90% yield. Chromatography on thick layer (2 mm silica gel) and subsequent molecular distillation afforded a water white oil which crystallized on cooling to 5°. The product was identical in all respects with the product obtained on pg 19.

Reaction of 1-Acetylhexene with Unstabilized Divinyl-copperlithium.

To purified cuprous iodide <sup>20</sup> (12.2 g; 60 mmole) suspended in dry THF (50 ml) at -78° was slowly added a solution of vinyl lithium in THF (120 mmole) while maintaining the temperature below -50°. The resultant deep green solution was stirred for 1 hr at -78°, and 1-acetylhexene (4 g; 32 mmole) in THF (50 ml) was slowly added keeping the temperature below -50°. The solution was stirred overnight at -30° and then quenched by pouring into saturated  $\text{NH}_4\text{Cl}$  solution (exothermic). The aqueous phase



was extracted with ether ( $2 \times 50$  ml). The combined organic phase was dried ( $\text{Na}_2\text{SO}_4$ ) and made up to 50 cc in a volumetric flask. Glc examination (5% SE30;  $100^\circ$ ) showed greater than 30% 1-acetylcyclohexene present. A yield of approximately 30% of the conjugate adduct, 2-vinyl-1-acetyl-cyclohexane, was found by glc.

Reaction of 1-Acetylcyclohexene with Tri-*n*-butylphosphine-Stabilized Divinylcopperlithium.

Tetrakis[iodo-(tri-*n*-butylphosphine)copper(I)] (23.6 g; 60 mmole) in THF (50 ml) was treated with a solution of vinyl lithium in THF (120 mmole) maintaining the temperature between  $-70^\circ$  to  $-50^\circ$ . 1-Acetylcyclohexene (3.7 g; 30 mmole) dissolved in THF (40 ml) was added slowly to the resultant blue-black solution over 0.5 hr. After stirring an additional 0.25 hr an aliquot was hydrolysed (saturated  $\text{NH}_4\text{Cl}$ ), dried ( $\text{Na}_2\text{SO}_4$ ) and examined by infrared spectroscopy. Shift of carbonyl absorption from 1680 to  $1710 \text{ cm}^{-1}$  indicated complete consumption of starting enone. The reaction mixture was quenched with saturated  $\text{NH}_4\text{Cl}$ . The aqueous phase was extracted with pentane ( $3 \times 30$  ml) and the combined organic phase was dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated. The yield of 2-vinyl-1-acetylcyclohexane in the residue was determined as 70% by glc (5% SE30;  $120^\circ$ ). A sample of this was isolated by preparative glc (10% SE30;  $135^\circ$ ); ir (thin film) 1705 ( $\text{C=O}$ ), 3080, 1635,  $910 \text{ cm}^{-1}$  ( $\text{CH}=\text{CH}_2$ );



nmr:  $\tau$  : 3.75-4.45 (m,1)  $\text{CH}_2=\text{CH}-$ , 4.90 (d,1)  $\text{HCH}=\text{CH}-$ , 5.12 (m,1)  $\text{HCH}-\text{CH}-$ , 7.92 (s,3)  $\text{CH}_3\text{C=O}$ , 7.20-8.8 (m,10)  $-\text{CH}(\text{CH}_2)_4-\text{CH}-$ ; mass spectrum  $m/e$ : 152(7), 137(6), 109(59), 97(11), 94(20), 81(22), 79(25), 67(80), 55(30), 43(100). Anal. Calcd. for  $\text{C}_{10}\text{H}_{16}\text{O}$ : C, 78.90; H, 10.59. Found: C, 78.84; H, 10.55.

Reaction of Cyclohex-2-en-1-one with Tri-*n*-butylphosphine-stabilized Divinylcopperlithium.

Tetrakis[iodo-(tri-*n*-butylphosphine)copper(I)] (11 g; 30 mmole) in THF (50 ml) was treated with a solution of vinyl lithium in THF (60 mmole) at -78°C. Cyclohex-2-en-1-one (1.43 g; 15 mmole), dissolved in THF (50 ml), was added over 0.25 hr and the resultant solution was stirred at -78° for 0.25 hr. An aliquot was quenched with saturated  $\text{NH}_4\text{Cl}$  solution. After drying ( $\text{Na}_2\text{SO}_4$ ) the aliquot was examined by infrared spectroscopy. Total shift of carbonyl from 1680 to 1710  $\text{cm}^{-1}$  indicated complete consumption of the starting enone. The remainder of the reaction mixture was treated with saturated  $\text{NH}_4\text{Cl}$ . The aqueous phase was extracted with pentane (4 x 30 ml) and the combined organic phase was dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated. The yield of 3-vinylcyclohexanone in the pale green residue was determined as 65% by glc (5% SE30; 100°). A sample was isolated by preparative glc (5% SE30; 120°); ir (thin film) 1710 (C=O), 3080, 1638, 912  $\text{cm}^{-1}$  ( $\text{CH}=\text{CH}_2$ ); nmr:  $\tau$  3.90-4.50 (m,1)



$\text{CH}_2=\text{CH}-$ , 4.90 (d,1)  $\text{HCH}=\text{CH}-$ , 5.15 (m,1)  $\text{HCH}=\text{CH}-$ , 7.4-9.0 (m,9)- $\text{CH}_2-$ ; mass spectrum  $m/e$ : 124(72), 109(10), 96(35), 95(15), 82(18), 81(100), 68(35), 67(75), 55(52), 54(62), 53(33), 41(42). Anal. Calcd. for  $\text{C}_8\text{H}_{12}\text{O}$ : C, 77.38; H, 9.74. Found: C, 77.29; H, 10.01.

Reaction of Methyl Vinyl Ketone with Tri-*n*-butylphosphine-stabilized Divinylcopperlithium.

Tetrakis[iodo-(tri-*n*-butylphosphine)copper(I)] (16.2 g; 41 mmole) in THF (50 ml) was treated with a solution of vinyl lithium in THF (82 mmole) at -78°. The resultant solution was stirred at -78° for 0.5 hr and methyl vinyl ketone (1.4 g; 20 mmole), dissolved in THF (20 ml), was added slowly over 0.3 hr. The solution was then stirred for 0.5 hr at -78° and quenched by pouring into saturated  $\text{NH}_4\text{Cl}$ . The two layers were separated and the aqueous was extracted with pentane (3 x 50 ml). The combined organic phase was dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated to yield a yellow residue which contained 69% 5-hexen-2-one by glc (15% SE30; 100°). A sample was isolated by preparative glc (15% SE30; 115°)  $n_D^{17} = 1.4182$  (lit.<sup>23</sup>  $n_D^{25} = 1.4178$ ; ir (thin film) 1715 (C=O), 3080, 1645, 910  $\text{cm}^{-1}$  ( $\text{CH}=\text{CH}_2$ ); nmr:  $\tau$  3.85-4.50 (m,1)  $\text{CH}_2=\text{CH}-$ , 4.90 (d,1)  $\text{HCH}=\text{CH}-$ , 5.15 (m,1)  $\text{HCH}=\text{CH}-$ , 7.61 (m,4)  $\text{CH}_2-\text{CH}_2$ , 7.9 (s,3)  $\text{CH}_3\text{C=O}$ ; mass spectrum  $m/e$ : 98(2.8), 8.3(2), 69(2) 55(7.5), 43(100), 41(4), 39(3.5).



Reaction of Isophorone with Tri-*n*-butylphosphine-stabilized  
Divinylcopperlithium.

Tetrakis[iodo-(tri-*n*-butylphosphine)copper(I)] (18 g; 45 mmole) in THF (50 ml) was treated with a solution of vinyllithium in THF (90 mmole) at -78°. After stirring at this temperature for an additional 0.5 hr, the solution was treated with isophorone (2.9 g; 21 mmole) dissolved in THF (25 ml). The reaction mixture was warmed to 0° and stirred at this temperature for 1 hr. The reaction mixture was then quenched by pouring into saturated NH<sub>4</sub>Cl solution and the two layers separated. The aqueous phase was extracted with pentane (2 x 50 ml) and the combined organic phase was dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated. Glc analysis of the residue (5% SE30; 120°) indicated an 85% yield of 3-vinyl-3,5,5-trimethylcyclohexanone. The crude reaction mixture was then chromatographed on silicic acid (Mallinkrodt) using Skelly B, and subsequently chloroform as eluants to give the 1,4-adduct as a yellowish oil. Upon distillation 3-vinyl-3,5,5-trimethylcyclohexanone was obtained as a clear liquid b.p. 132-135° (34 mm),  $n_D^{25}$  1.4655 in 60% yield; ir (thin film) 1710 (C=O), 3080, 1635, 910 cm<sup>-1</sup> (CH=CH<sub>2</sub>); nmr  $\tau$ : 3.90-4.50 (m,1) CH<sub>2</sub>=CH-, 5.10 (m,2) CH<sub>2</sub>=CH-, 7.62 (q,2) COCH<sub>2</sub>C(CH<sub>3</sub>)CH=CH<sub>2</sub> 7.85 (s,2) CO-CH<sub>2</sub>C(CH<sub>3</sub>)<sub>2</sub>, 8.31 (s,2) (CH<sub>3</sub>)<sub>2</sub>C-CH<sub>2</sub>-HC(CH<sub>3</sub>)CH=CH<sub>2</sub>, 8.92 (s,3) CH<sub>3</sub>-C-CH=CH<sub>2</sub>, 8.99 (s,3) (CH<sub>3</sub>)<sub>2</sub>C, 9.02 (s,3) (CH<sub>3</sub>)<sub>2</sub>C; mass spectrum  $m/e$ :



166(35), 151(20), 138(8), 109(32), 95(46), 83(85) 82(76),  
68(60), 67(100), 56(40), 55(65). Anal. Calcd. for  $C_{11}H_{18}O$ :  
C, 79.46; H, 10.91. Found: C, 79.68; H, 11.30.

Reaction of Tri-*n*-butylphosphine-stabilized Divinylcopper-lithium with Mesityl Oxide.

Tetrakis[iodo(tri-*n*-butylphosphine)copper(I)] (4.7 g; 12.5 mmole) in THF (25 ml) was treated with a solution of vinyl lithium in THF (25 mmole) at -78°. The resultant solution was stirred at -78° for 0.5 hr. Mesityl oxide (0.6 g; 6.2 mmole) in THF (10 ml) was added slowly at -78° (0.5 hr) and the solution was allowed to warm to 0°. After stirring at this temperature for 2 hrs, an aliquot was withdrawn, hydrolysed (saturated  $NH_4Cl$ ), dried ( $Na_2SO_4$ ) and examined by infrared. The carbonyl absorptions at  $1680\text{ cm}^{-1}$  had completely disappeared indicating the reaction was complete. The reaction mixture was quenched by pouring into saturated  $NH_4Cl$ . The aqueous phase was extracted with pentane (2 x 50 ml) and the combined organic phase was dried ( $Na_2SO_4$ ) and evaporated. The yield of 4,4-dimethyl-5-hexen-2-one in the yellow residue was 72% by glc (5% SE30; 60°). The residue was chromatographed on silicic acid (Mallinkrodt) using Skelly B and subsequently chloroform as eluant. The carbonyl-containing fraction was subjected to distillation and afforded 4,4-dimethyl-5-hexen-2-one, b.p. 75° (60 mm) [(lit.<sup>24</sup> 69-75 (60 mm)]; ir (thin film) 1710 (C=O), 3020, 1610, 910  $\text{cm}^{-1}$  ( $CH=CH_2$ ); nmr  $\tau$



3.65-4.30 (m,1)  $\text{CH}_2=\text{CH}-$ , 4.80 (d,1)  $\text{HCH}=\text{CH}-$ , 5.10 (m,1)  $\text{HCH}=\text{CH}-$ , 7.55 (s,2)  $\text{CH}_2-\text{C=O}$ , 7.85 (s,3)  $\text{CH}_3\text{C=O}$ , 8.89 (s,6)  $\text{CH}_3\text{C-CH}_3$ ; mass spectrum m/e: 126 (2.7), 111 (6.3), 83 (15), 69 (25), 55 (20), 43 (100), 41 (41), 39 (15).

Copper-catalysed Reaction of Vinylmagnesium Bromide with Isophorone.

Vinylmagnesium bromide <sup>21</sup> (72 mmole) in THF (100 ml) was treated at 0° with 10 mole percent cuprous iodide (1.5 g). The mixture was stirred at this temperature for 0.5 hr and then isophorone (5.1 g; 37 mmole) in THF (30 ml) was added slowly. After being stirred for 1 hr the mixture was quenched by pouring into saturated  $\text{NH}_4\text{Cl}$ . The two layers were separated and the aqueous phase was extracted with ether (3 x 30 ml). The combined organic phase was dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated. The yield of 3-vinyl-3,5,5-trimethylcyclohexanone in the residue was 8.6% by glc (5% SE30; 65°). A sample obtained by preparative glc (5% SE30; 130°) proved to be identical in all respects with the compound obtained on pg 24. A white precipitate separated from the yellow residue on standing; this was filtered off and recrystallized from acetone:ether (1:1 by volume) to afford bi-1,5,5-trimethyl-3-oxocyclohexyl, m.p. 167-168° in 7% yield; ir ( $\text{CHCl}_3$ )  $1705 \text{ cm}^{-1}$  (C=O); nmr  $\tau$  7.79 (q,2)  $\text{CH}_2-\text{C-}$ , 7.85 (s,2)  $\text{CH}_2-\text{C=O}$ , 8.41 (q,2)  $\text{CH}_2-\text{C}$ ,



8.94(s,6)  $\text{CH}_3\text{-C-CH}_3$ , 8.97(s,3)  $\text{CH}_3\text{-C-}$ ; mass spectrum m/e:  
 278(0.3), 263(0.72), 245(0.65) 207(0.67), 189(0.57),  
 165(0.55), 140(24), 139(100), 125(28), 83(50), 69(15),  
 55(49). Anal. Calcd. for  $\text{C}_{18}\text{H}_{30}\text{O}_2$ : C, 77.65; H, 10.86.  
 Found: C, 78.10; H, 10.94.

Copper-catalysed Reaction of Vinylmagnesium Bromide with Mesityl Oxide.

Vinylmagnesium bromide <sup>21</sup> (60 mmole) in THF (50 ml) was treated at 0° with 5 mole percent (0.47 g; 3 mmole) cuprous iodide and stirred at this temperature for 0.5 hr. Mesityl oxide (2.96 g; 30 mmole) in THF (25 ml) was added slowly and the resultant solution stirred at 5° for 1.75 hr. The mixture was then quenched by pouring into saturated  $\text{NH}_4\text{Cl}$  and the two layers were separated. The aqueous phase was extracted with ether (2 x 50 ml) and the combined organic phase was dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated. The yield of 4,4-dimethyl-5-hexen-2-one in the residue was 7% by glc (5% SE30; 60°). A sample isolated by preparative glc (5% SE30; 70°) was identical in all respects with the compound obtained on p. 25.

Copper-catalysed Reaction of Vinylmagnesium Bromide with Cyclohexenone.

Vinylmagnesium bromide <sup>21</sup> (50 mmole) in THF (50 ml) was treated at 0° with 5 mole percent (.40 g; 2.5 mmole) cuprous iodide and the resultant deeply coloured mixture



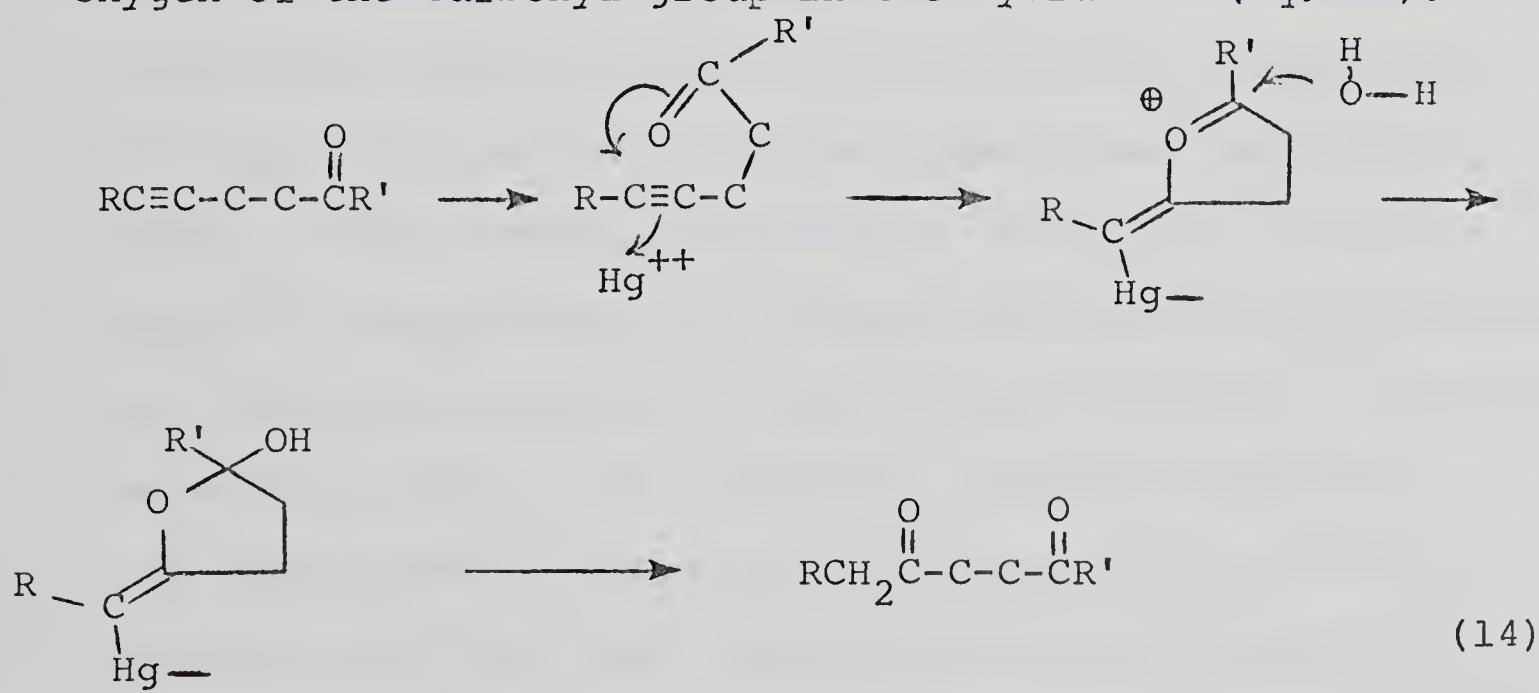
was stirred at this temperature for 0.5 hr. 2-Cyclohexenone (2.45 g; 25 mmole) in THF (75 ml) was added slowly and the mixture was stirred for 1 hr. The reaction was quenched by pouring into saturated  $\text{NH}_4\text{Cl}$  solution and the two layers separated. The aqueous phase was extracted with ether (2 x 50 ml) and the combined organic phase was dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated. The yield of 3-vinylcyclohexanone in the residue was 69% by glc (5% SE30; 90°). A sample was isolated by glc (5% SE30; 120°) and proved to be identical in all respects with the compound obtained on pg 22.



THE REACTION OF DIALKYLALKYNYLALANE REAGENTS WITH CONJUGATED ENONES. A METHOD FOR THE 1,4-ADDITION OF ACETYLENE UNITS TO  $\alpha$ ,  $\beta$ -UNSATURATED KETONES

I N T R O D U C T I O N

$\gamma$ ,  $\delta$ -Acetylenic ketones are highly valued synthetic intermediates since functionality arrangement of this type permits easy access to an assortment of important structural classes. Stork and Borch have shown that the acetylenic bond will selectively hydrate in the presence of catalytic quantities of mercuric salts to give 1,4-diketones.<sup>26</sup> He attributes this selectivity to a participation by the oxygen of the carbonyl group in the hydration (eq. 14).

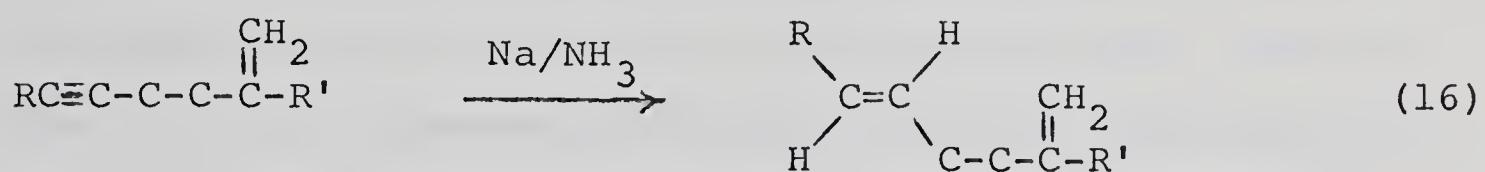


Johnson and coworkers have demonstrated that these compounds can be readily converted, using standard methods, to 1,5-dienes.<sup>27</sup> First a Wittig reaction is performed:



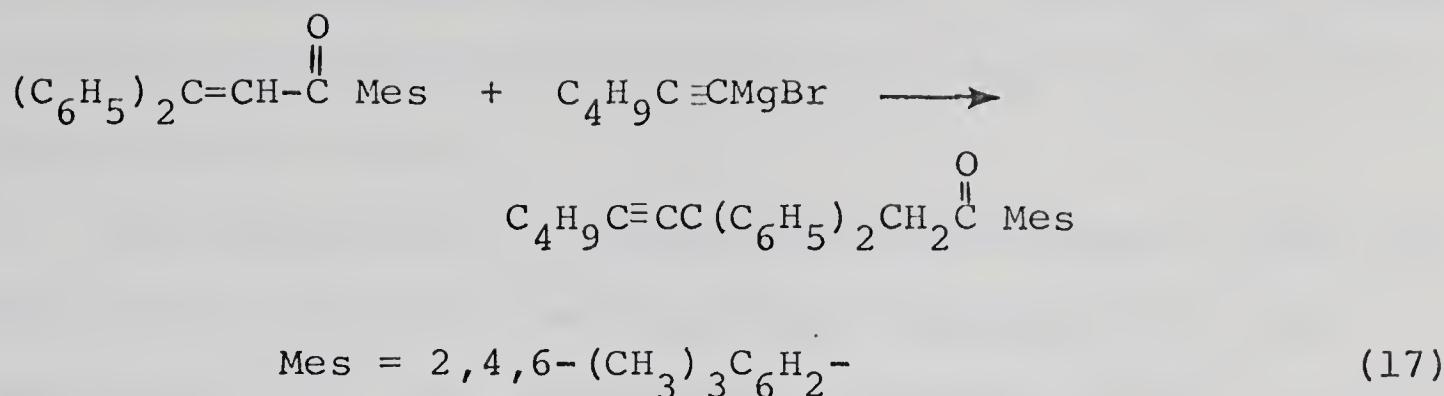


and then by adding (inverse addition) the enyne product to a solution of sodium in liquid ammonia the desired 1,5-diene is obtained in good yield and high isomeric purity:



Conceptually the most direct approach to the synthesis of these  $\gamma$ ,  $\delta$ -acetylenic ketones involves a Michael-type reaction between an acetylenic unit and a conjugated enone. In practise, however, most attempts at this 1,4-addition have been unsuccessful. It has already been mentioned in Chapter I that Normant succeeded in adding an acetylenic moiety to the  $\beta$ -carbon of a doubly activated, cross-conjugated  $\alpha$ ,  $\beta$ -unsaturated system.<sup>5</sup> Rea<sup>10</sup> has undertaken a study of the mode of addition of acetylenic Grignard reagents to  $\alpha$ ,  $\beta$ -unsaturated ketones in the presence and absence of catalysts and found that only one substrate afforded an acceptable yield of the conjugate adduct. Benzalacetomesitylene appears to have such great steric hindrance to 1,2-addition at the carbonyl group that a 92% yield of the 1,4-addition product is obtained, even in the absence of any catalyst.

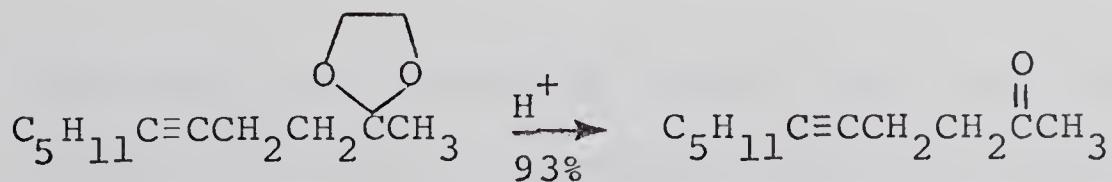
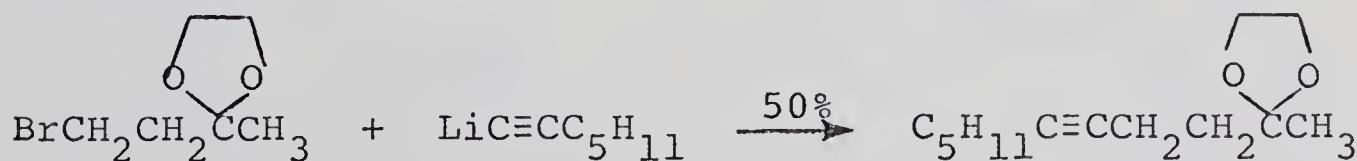
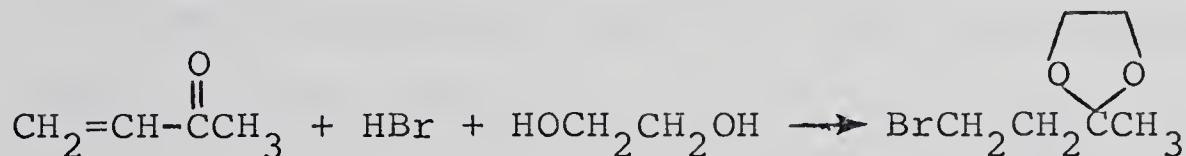




Credence is lent to the idea that this is a steric phenomenon by the observation of Nesmeyanov that the even more reactive organometallic, phenyllithium,\* also adds conjugately to this enone in 90% yield.<sup>36</sup>

In general, though, Rea found that  $\alpha,\beta$ -unsaturated ketones afforded good yields of the 1,2-adducts both with or without catalysis using acetylenic Grignard reagents.

Stork obtained his desired  $\gamma,\delta$ -acetylenic ketones by a two-step sequence:<sup>26</sup>



Johnson's attempts at adding an acetylenic Grignard

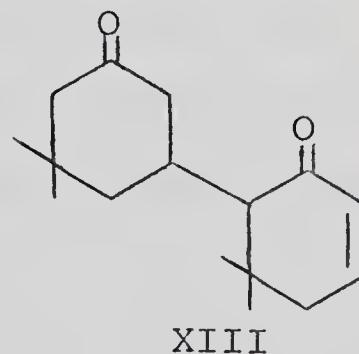
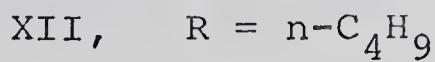
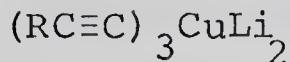
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\* Usually alkylolithium compounds add 1,2- to conjugated enones.



to a conjugated enone were unsuccessful<sup>27</sup> and he was forced to resort to a multi-step procedure to obtain the desired  $\gamma,\delta$ -acetylenic ketone.

The propensity of organocopper derivatives to add conjugately to  $\alpha,\beta$ -unsaturated carbonyl substrates for the appendage of  $\text{sp}^3$ - and  $\text{sp}^2$ -hybridized moieties<sup>15,28</sup> suggested the possibility of alkynylcuprates accomplishing this addition for an sp-hybridized species. Consequently this approach was investigated at the outset of this project. However, results were unrewarding. Subsequent to this investigation House published the results of an examination of the reaction of trialkynylcopperlithium species (to form a soluble cuprate, House found it necessary to react three equivalents of alkynyllithium salt with one of cuprous iodide<sup>14</sup>) with enone systems.<sup>29</sup> Reaction of XI or XII with 5,5-dimethylcyclohex-2-en-1-one led to predominantly a dimeric ketone (XIII).

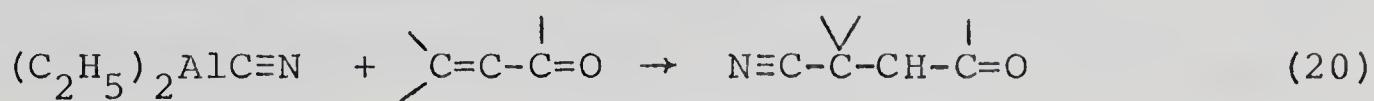


(19)

This diketone presumably arises from the formation of an enolate ion from the starting enone and subsequent Michael addition of this ion to a second molecule of starting material.



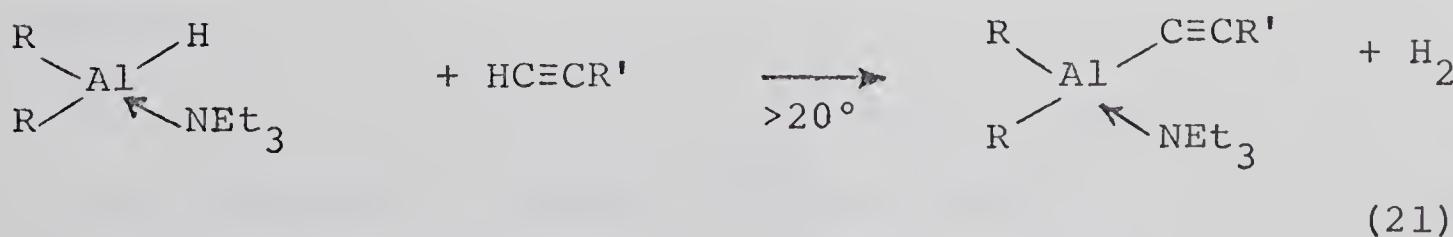
It thus becomes obvious that no satisfactorily general method exists for the attachment of an acetylenic moiety to the  $\beta$ -carbon of an enone system. There is, however, a method documented in the literature which successfully transfers an sp-hybridized carbon atom conjugately to an enone. Nagata has employed a cyanoaluminum reagent to deliver the sp-hybridized carbon atom of a cyano function to the  $\beta$ -carbon of an enone<sup>30</sup> *viz.*



The aluminum reagent was readily prepared by the reaction of HCN with triethylaluminum.

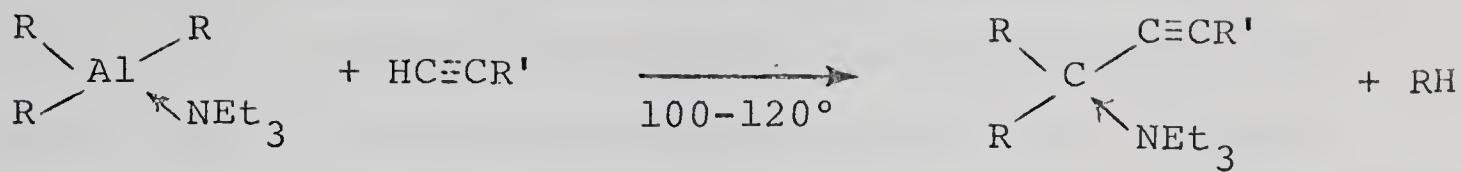
The possibility thus arose of employing the alkynyl analogue to the Nagata reagent to effect the conjugate addition of an alkynyl group to an  $\alpha,\beta$ -unsaturated ketone. Species of the type  $R_2AlC\equiv CR'$  had in fact been synthesized.

Binger<sup>31</sup> showed that dialkylaluminum hydrides and trialkylaluminum compounds react with terminal acetylenes in the presence of triethylamine to give good yields of the dialkylalkynylalane (eq. 21).



or





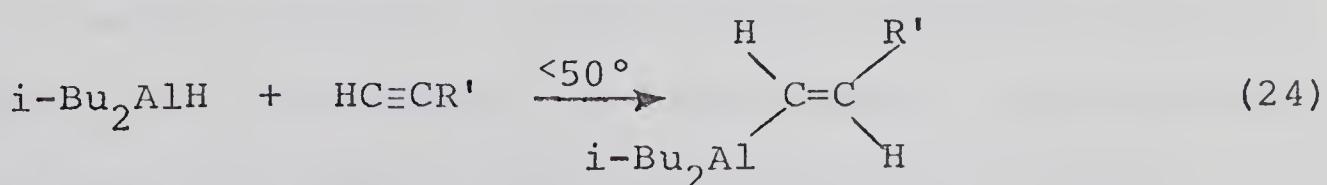
Fried and coworkers prepared the dialkylalkynylalanes in quantitative yield by reacting an acetylide salt with a dialkylaluminum halide <sup>32</sup> (eq. 22).



Organoaluminum compounds in which the carbon atoms attached to aluminum have different hybridization (dialkylalkynyl, di- and trialkylalkenyl) prefer to "transfer" that ligand whose attaching carbon atom has the highest degree of "s" character. When reacting a dialkylalkynylalane with a series of epoxides Fried and coworkers found that in all cases the alkynyl alcohol resulting from migration of the acetylenic moiety was the sole product:<sup>32</sup>



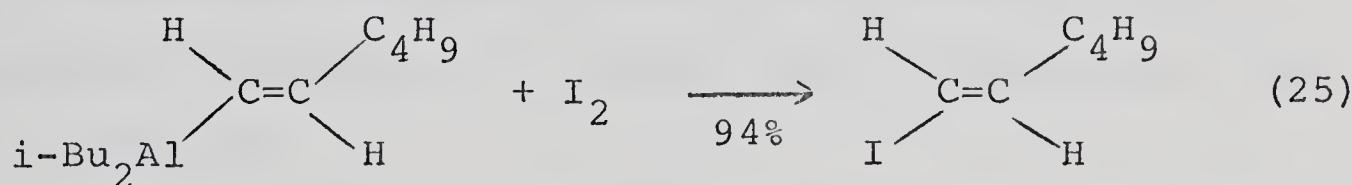
Zweifel and coworkers have shown that dialkylalkenylalanes are readily available by the hydroalumination of acetylenes:



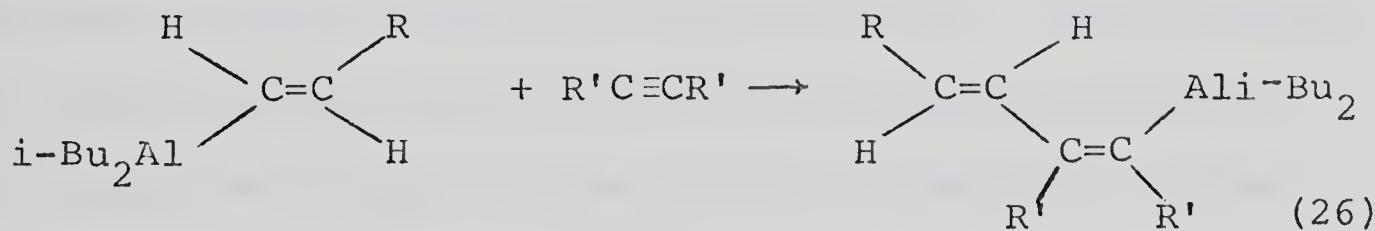


A *cis* addition of the aluminum-hydrogen bond to the triple bond is involved to yield *trans*-vinylalanes from 1-alkynes and *cis*-vinylalanes from disubstituted alkynes.

Vinylalanes can be subjected to a variety of reactions and in all cases it is the vinylcarbon-aluminum bond which cleaves. For example, reaction with halogens<sup>33</sup> gives, in excellent yields, a straightforward synthesis of the corresponding vinyl halide:



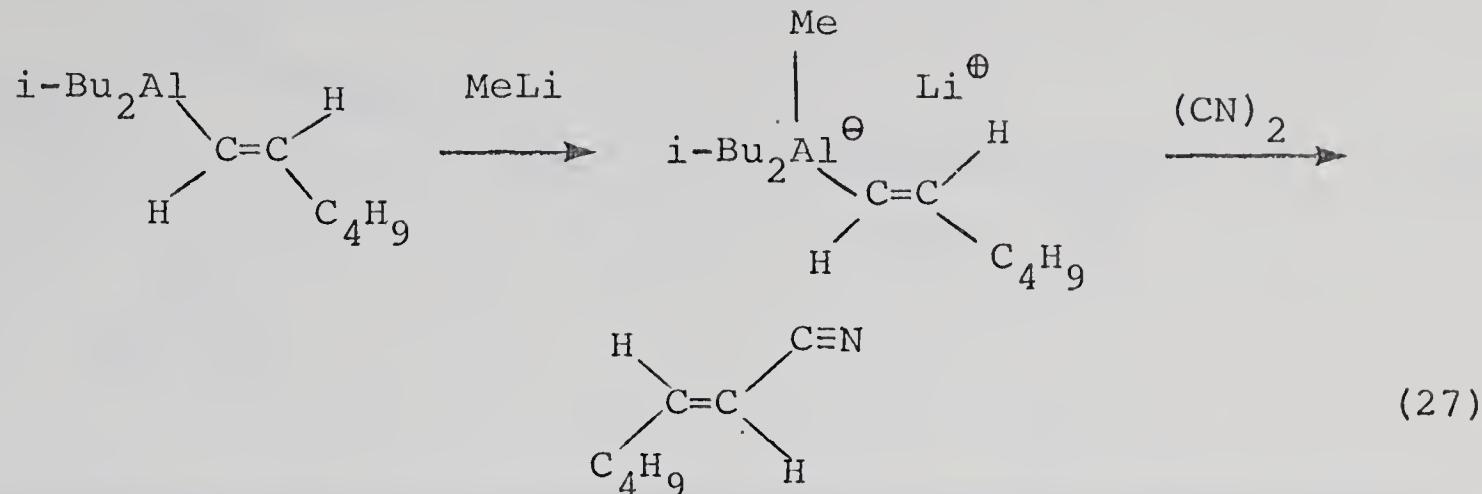
They also react with carbon dioxide,<sup>34</sup> and will add across triple bonds to produce dienes<sup>35</sup> upon hydrolysis.



If the vinylalane is first converted to the "ate" complex by the addition of an equivalent of alkylolithium reagent, the yields in the carbonation reaction are much higher. In addition, this process renders the vinylalane reactive towards cyanogen<sup>35</sup> and carbonyl compounds such as acetaldehyde and paraldehyde. In this manner,  $\alpha,\beta$ -unsaturated nitriles and alcohols have been produced in good

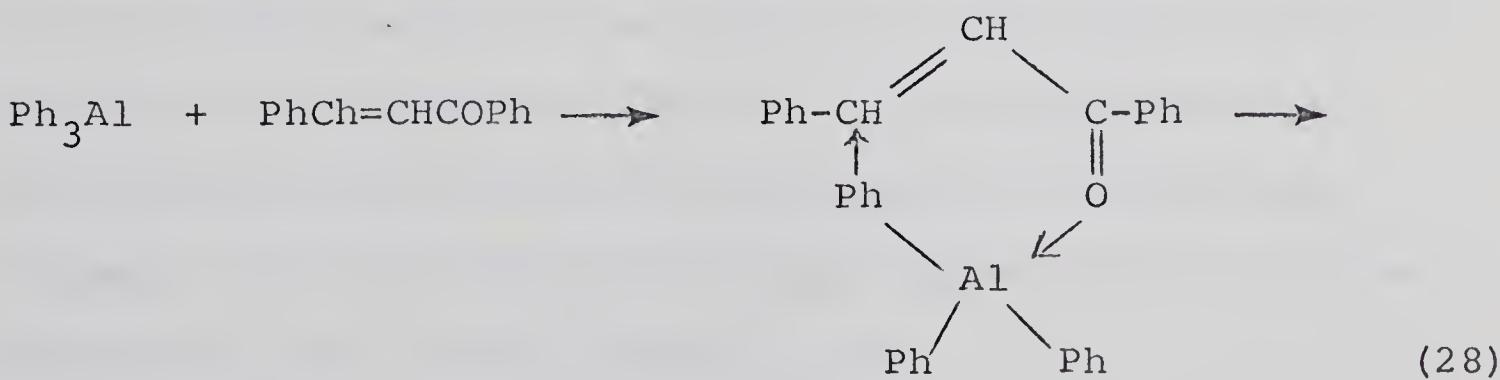


yields.



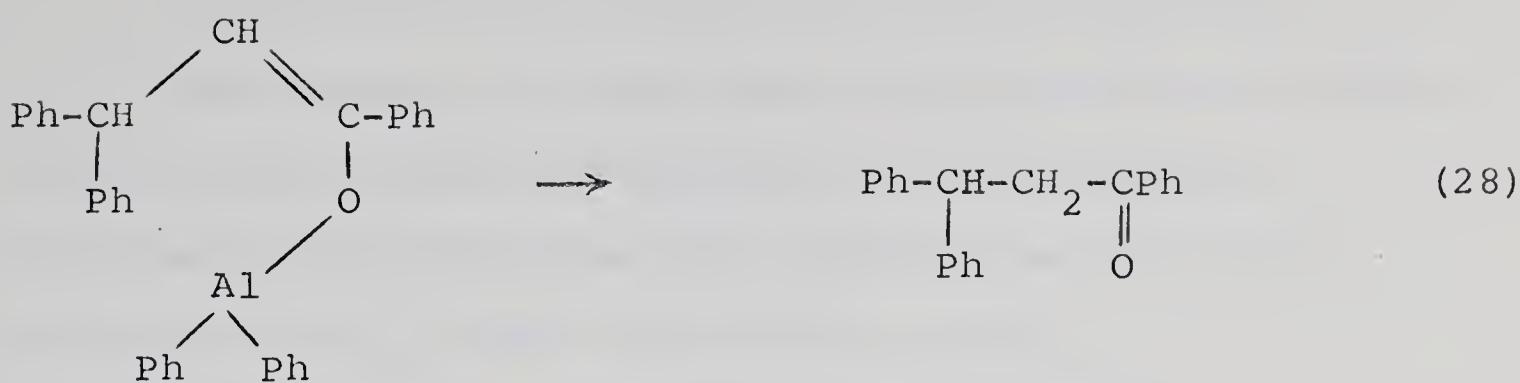
Of the four aluminum-carbon bonds present in the intermediate aluminate it is again the Al-vinylcarbon bond that is cleaved.

Recently trialkylaluminum compounds have been reacted with  $\alpha,\beta$ -unsaturated carbonyl systems.<sup>37,38</sup> Baba<sup>37</sup> reports that the very reactive triethylaluminum adds in a 1,2-fashion to conjugated enones. Attempts at maximizing 1,4-addition by adding different ethers failed. Wittig and Bub have reacted triphenylaluminum with benzalacetophenone<sup>39</sup> and realized excellent yields of the 1,4-adduct. These workers attribute this to the formation of an intermediate "ate" complex (XIV)



XIV





and reason that it is because phenylsodium or phenyllithium are unable to form this "ate" complex, that the latter effect 1,2-addition to the same substrate. Baba, on the other hand, points out that because triethylaluminum is still capable of forming such an "ate" complex and yet adds 1,2 to the conjugated enone, the conjugate addition of triphenylaluminum to benzalacetophenone must be due to the lower reactivity of this organometallic.

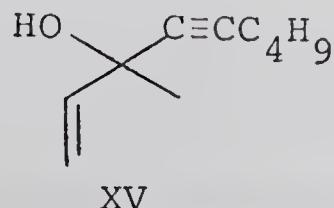
The bonding of an alkynyl moiety to an aluminum atom in an alane should attenuate its reactivity relative to that of a trialkylalane and thus favour 1,4- as opposed to 1,2-addition of the preferentially migrating alkynyl group to a conjugated enone system. Consequently, the purpose of the present work was to investigate the possibility of achieving the conjugate addition of an alkynyl moiety to an  $\alpha,\beta$ -unsaturated ketone by employing an alkynylalane reagent. The reaction of an alkynylcuprate with an enone system was also briefly investigated.



## R E S U L T S   A N D   D I S C U S S I O N

The success of alkyl- and alkenylcuprates at effecting conjugate addition suggested the possibility of utilizing alkynylcuprates for attaching an acetylenic moiety to the  $\beta$ -carbon of an enone system.

Using the stoichiometry already established for the formation of alkyl- and alkenylcuprates, two equivalents of a lithium acetylide were added to a suspension of one equivalent of cuprous iodide in THF at  $-78^\circ$ . A voluminous grey precipitate immediately formed, reminiscent of Gilman's original observation on the formation of polymeric methyl-copper.<sup>11</sup> Methyl vinyl ketone was then added at  $-78^\circ$ . The progress of the reaction was monitored by infrared spectroscopy and after 2.5 hr the starting material had been completely consumed. The disappearance of the carbonyl peak of starting material at  $1680\text{ cm}^{-1}$  was, however, accompanied by the appearance of considerable hydroxyl absorption at  $3500\text{ cm}^{-1}$  as well as only a minor amount of carbonyl absorption at  $1710\text{ cm}^{-1}$ . When the hydrolysed reaction mixture was examined by glc there was a negligible amount of 5-decyn-2-one detected. Distillation of the reaction mixture afforded greater than 60% of the 1,2-adduct, 3-methylnon-1-en-4-yn-3-ol (XV).





The addition of two mole equivalents of an acetylide salt to one of cuprous iodide has since been reported by House to yield a heterogeneous mixture.<sup>14,29</sup> The addition of a further mole equivalent of acetylide salt results in a homogeneous solution. Because of this observation House has formulated the alkynylcuprate as a trialkynylcopper-dilithium species, in marked contrast to the already reported dialkyl- and dialkenylcopperlithium reagents.<sup>12,14</sup> The alkynylcuprate, however, fails to add conjugately to an enone system.<sup>29</sup>

Because of the unpromising result observed in the above reaction with methyl vinyl ketone, and in the light of House's failure to achieve conjugate addition with dilithium trialkynylcuprates, it was decided to discontinue this investigation and to turn attention instead to a study of the applicability of a dialkylalkynylalane as a reagent for achieving the conjugate addition of an alkynyl group.

The desired alane reagent was prepared by a slight modification of the procedure of Fried and coworkers.<sup>32</sup> They treated a solution of lithium acetylide in toluene with an equivalent amount of a solution of diethylaluminum chloride in toluene. This exothermic reaction led to the precipitation of LiCl and formation of the desired reagent.



Ligroin was initially chosen as solvent for the pre-



paration of the alane in this study. Addition of a commercially available solution of *n*-butyllithium in hexane to an equimolar amount of 1-hexyne in ligroin was exothermic and resulted in the formation of a gelatinous suspension of the acetylide salt. Addition of an equimolar amount of diethylaluminum chloride dissolved in ligroin was not exothermic and resulted in no change in the overall appearance of the reaction mixture, even after stirring for several hours. It was thought that the reason for the lack of reaction might be the insolubility of the lithium acetylide in ligroin. Addition of as little as 10% ether (by volume) at this point resulted in an exothermic reaction which changed the appearance of the suspended white solid from an amorphous suspension to a finely divided crystalline precipitate. Cessation of stirring allowed this precipitate to settle out and left a clear, colourless supernatant. Presumably then, the small amount of added ether provided a common phase for reaction between the ligroin-insoluble acetylide salt and the diethylaluminum chloride.

The decanted supernatant was treated with 0.5 mole equivalent of 1-acetylhexene and after stirring for 1 hr examination of the hydrolysed reaction mixture by infrared spectroscopy indicated complete consumption of starting enone. The yield of the 1,4-addition product, 2-(1-hexynyl)-acetylhexene in the worked up reaction mixture was estimated as 85% by glc.



In order to assess the general applicability of this reaction for acetylenes, diethylphenylethynylalane was prepared from phenylacetylene using a procedure similar to that described above for diethylhexynylalane. Upon reaction with 0.5 mole equivalents of 1-acetylhexene for 1.5 hr, workup and examination of the residue by glc indicated a 71% yield of the 1,4-adduct, 2-(phenylethynyl)acetylhexane.

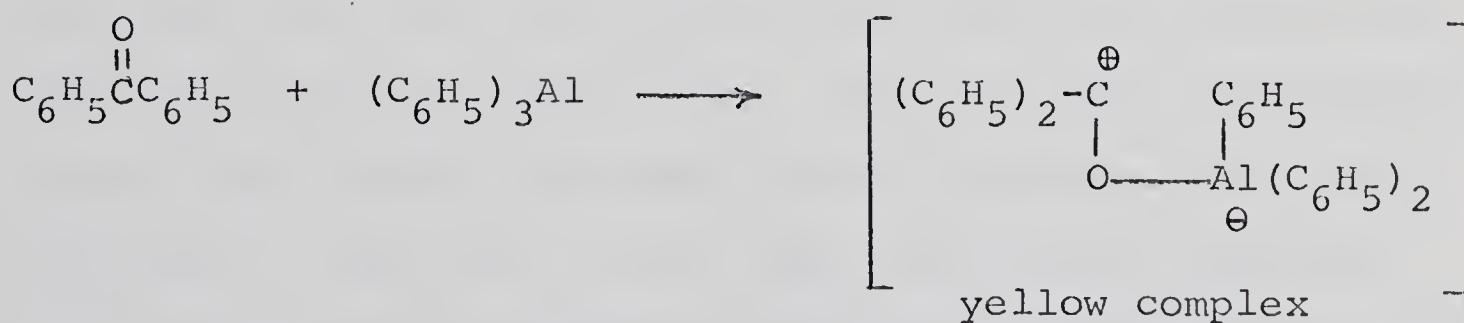
This success led to the examination of the reaction with another enone substrate. The diethylhexynylalane was again prepared in a 10:1 ligroin:ether solvent system and decanted from the precipitated LiCl. Methyl vinyl ketone dissolved in ligroin was added at room temperature ( $25^{\circ}$ ) and again the addition was accompanied by the appearance of a yellow colouration which rapidly diffused. After stirring for 0.75 hr hydrolysis and examination of an aliquot by infrared spectroscopy showed the appearance of a band at  $1710\text{ cm}^{-1}$  along with total disappearance of the starting material absorption at  $1680\text{ cm}^{-1}$ . The reaction mixture was worked up and glc examination of the crude product indicated a 54% yield of 5-decyn-2-one, the expected conjugate adduct.

The lower yield of 1,4-addition product in this reaction might be due to polymerization of the enone in the presence of the alane. (Lyons<sup>38</sup> reports the efficient polymerization of methyl isopropenyl ketone in the presence of triethylaluminum). Alternatively some form of condensation

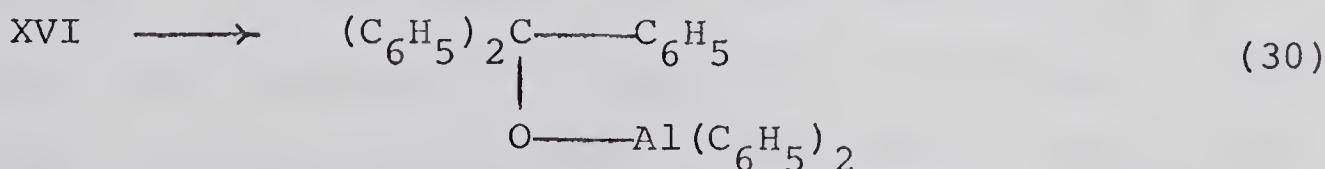


process<sup>37</sup> might be consuming the starting material before it can be converted into the desired product. One could hopefully overcome both these problems by attenuating the reactivity of the alane reagent. Lowering the reaction temperature would be one method to achieve this end. Another possible modification would be to introduce a solvent such as THF into the reaction mixture. The basis of the rationale for the latter conclusion was as follows.

Wittig studied the reaction of benzophenone with triphenylaluminum and observed that a yellow complex was formed immediately upon addition of the ketone to the organometallic reagent. He suggested<sup>39</sup> that this colouration was due to the formation of a complex between the ketone and the aluminum reagent which subsequently decomposed to product (eq. 30)



XVI



Ashby and coworkers observed a similar colouration upon the



addition of benzophenone to trimethylaluminum,<sup>37</sup> and Lyons reported a similar phenomenon when methyl isopropenyl ketone was added to triethylaluminum.<sup>38</sup> The colourations observed upon the addition of 1-acetylcyclohexene and methyl vinyl ketone to the diethylalkynylalane also might be indicative of the same phenomenon. Consequently, the addition of a Lewis base, such as THF, to the reaction medium might be expected to compete with the carbonyl oxygen of the enone for the alane Lewis acid, and thereby possibly affect the outcome of reaction. Tetrahydrofuran is known to be a stronger Lewis base than ethyl ether and thus was chosen as the additive.

Consequently diethylhexynylalane was prepared in a THF:ligroin solvent system, and after being decanted from the precipitated LiCl under nitrogen, was cooled to -78°. (It should be noted that if the concentration of the alkynylalane was less than 0.25 M in THF the LiCl would not precipitate from the reaction mixture<sup>42</sup>). One half mole equivalent of methyl vinyl ketone was added to this solution, and after stirring at -78° for 1.75 hr, the reaction was quenched. Examination of the reaction mixture by glc showed 70% methyl vinyl ketone remained unreacted, but no 5-decyn-2-one could be detected. It was apparent that the reactivity of the alane had been attenuated but possibly by too great a degree.

The reaction was repeated in THF at 0°. After stirring for 2.5 hrs subsequent to the addition of methyl vinyl ketone the reaction was warmed to 25° and hydrolysed. The



absence of methyl vinyl ketone was confirmed by glc but again no trace of the conjugate adduct could be detected. The presence of THF in the reaction mixture had thus caused a decrease in yield of the 1,4-addition product from 54 to 0%.

In order to assess the effect of THF on the reaction of a dialkylalkynylalane with 1-acetylcyclohexene, diethyl-phenylethylnylalane was prepared as before and sufficient THF was added to the decanted supernatant to make the ratio of THF:ligroin approximately 2:1. The reaction mixture was cooled to -15° and 0.5 mole equivalent of 1-acetylcyclohexene was added. The reaction was stirred for 1.25 hr at which time hydrolysis of an aliquot and examination by infrared spectroscopy indicated total consumption of starting material. The remainder of the reaction mixture was hydrolysed and the amount of 2-(phenylethynyl)acetylcyclohexane present was shown to be only 3% by glc.

The low yield of the alkynyl conjugate adduct in this last reaction confirms the inadviseability of the use of THF as a solvent or cosolvent for the alkynylalane - enone reaction.

We then undertook to survey the reactions of a variety of  $\alpha,\beta$ -unsaturated ketones under some standard set of conditions in order to assess the general applicability of the alkynylalane in achieving the conjugate addition of the alkynyl moiety. The results of this survey will be found



in Table II. The conditions ultimately decided upon were based on the results previously obtained with 1-acetylcyclohexene. In general a dialkylalkynylalane (generated from the corresponding lithium acetylidyde and diethylaluminum chloride) was dissolved in an approximately 10 to 15:1 ligroin:ether solvent system. A 2:1 ratio of alane to enone substrate was used in all cases. The temperature of the reactions ranged from -15° to room temperature. This was determined by the low solubility of the alane in the ether:ligroin solvent system. At temperatures below -20° the alane began to separate from the reaction mixture as an oil. The use of lower temperature, however, did not seem to have any effect on the course of the reaction. For example, methyl vinyl ketone gave 54% of the conjugate adduct when the reaction was carried out at room temperature (25°) as opposed to 48% when the addition was done at -15°. 1-Acetylcyclohexene gave an 85% yield of the 1,4-addition product when the reaction was performed at room temperature while a 79% yield was afforded when the reaction temperature was 0°. The results recorded from reactions conducted at different temperatures are within the experimental error of their determination and must therefore be considered as comparable.

It is interesting to note that excellent yields were obtained for those enone systems in which the  $\beta$ -carbon was substituted with an aromatic ring. In the case of the



reaction of diethylhexynylalane with benzalacetophenone the isolated yield of 65% is probably quite low. Infrared examination of the crude reaction mixture showed negligible hydroxyl absorption (characteristic of the 1,2-adduct) but the conjugate adduct was a very high-boiling oil which seemed to decompose considerably during distillation, nor could it be analyzed by glc.

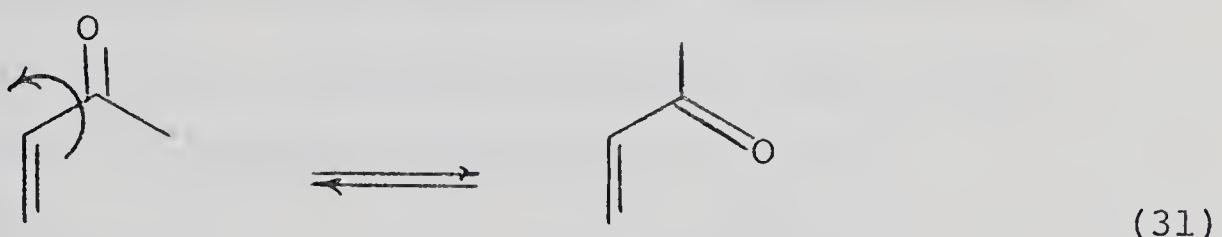
Those enones in which the  $\beta$ -carbon atom is unsubstituted (or substituted with non-aromatic groups) gave the lowest yields. In addition, the cyclic enones that were examined (2-cyclohexenone and isophorone) gave no conjugate adduct whatever. In order to better understand the nature of the reaction in the case of these enones an estimate was made of the amount of 1,2-adduct formed. The desired alcohols were made by direct reaction of the appropriate lithium acetylide with the  $\alpha,\beta$ -unsaturated ketone in THF. The results of this study are found in Table III.

It is interesting to note the amount of consumed enone which cannot be accounted for by conversion to either 1,2- or 1,4-adduct. There is approximately 30% of the starting enone lost to some other reaction. In his study of the reactions of  $\alpha,\beta$ -unsaturated carbonyl compounds with triethylaluminum, Baba reports that with mesityl oxide 66% is converted to 1,2-adduct, 0.3% to 1,4-adduct, and 26% to condensation product.<sup>37</sup> Possibly, then, this 30% of



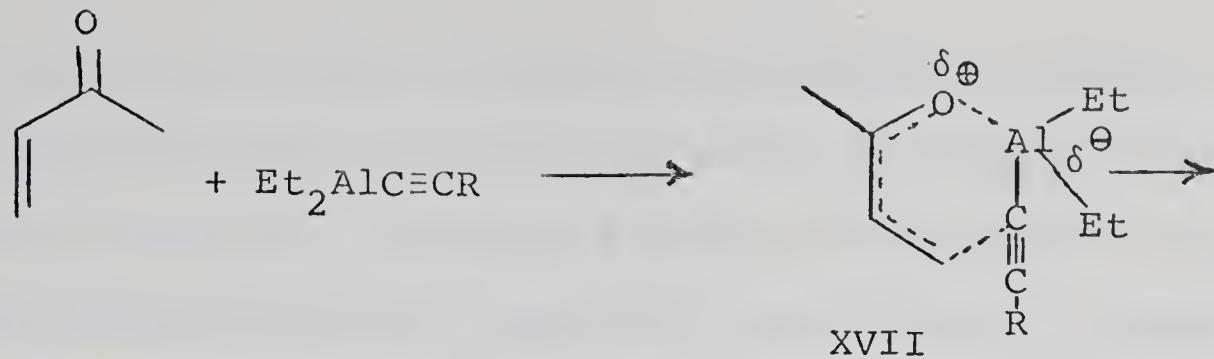
starting material is being converted to some form of condensation (or polymerization) product, although no investigation was made of this point.

A closer examination of the results in Table II reveals that although the cyclic enones 2-cyclohexenone and isophorone gave no 1,4-adduct, acyclic but similarly substituted analogues (pent-3-en-2-one and mesityl oxide) yielded 54% and 30% respectively of the respective conjugate adducts. The major structural difference between the cyclic and acyclic enones is the ability of the latter to rotate about the carbonylcarbon—vinylcarbon bond. As a result of this rotation these enones can achieve a *syn*-type orientation of the carbonyl group and the double bond (eq. 31).

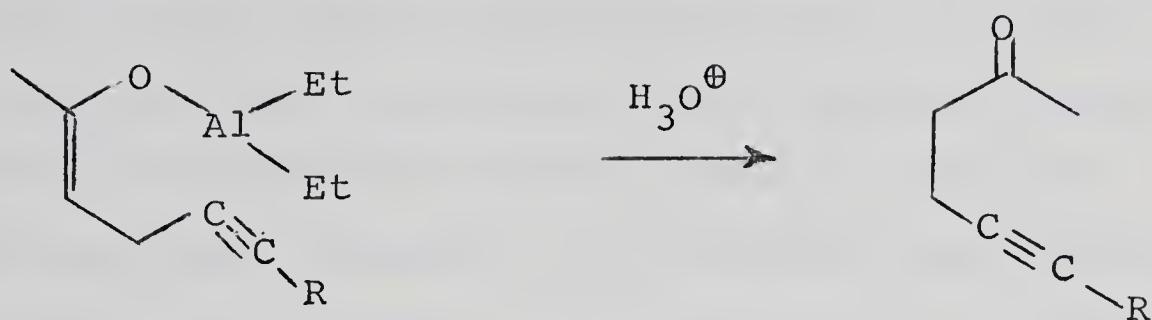


If the first step in the reaction with the alkynylalane involves complex formation between the carbonyl oxygen and the aluminum atom as Wittig<sup>39</sup> suggests it becomes readily evident that conjugate addition can be subsequently accomplished *via* a six-centred transition state (XVII) (eq. 32).

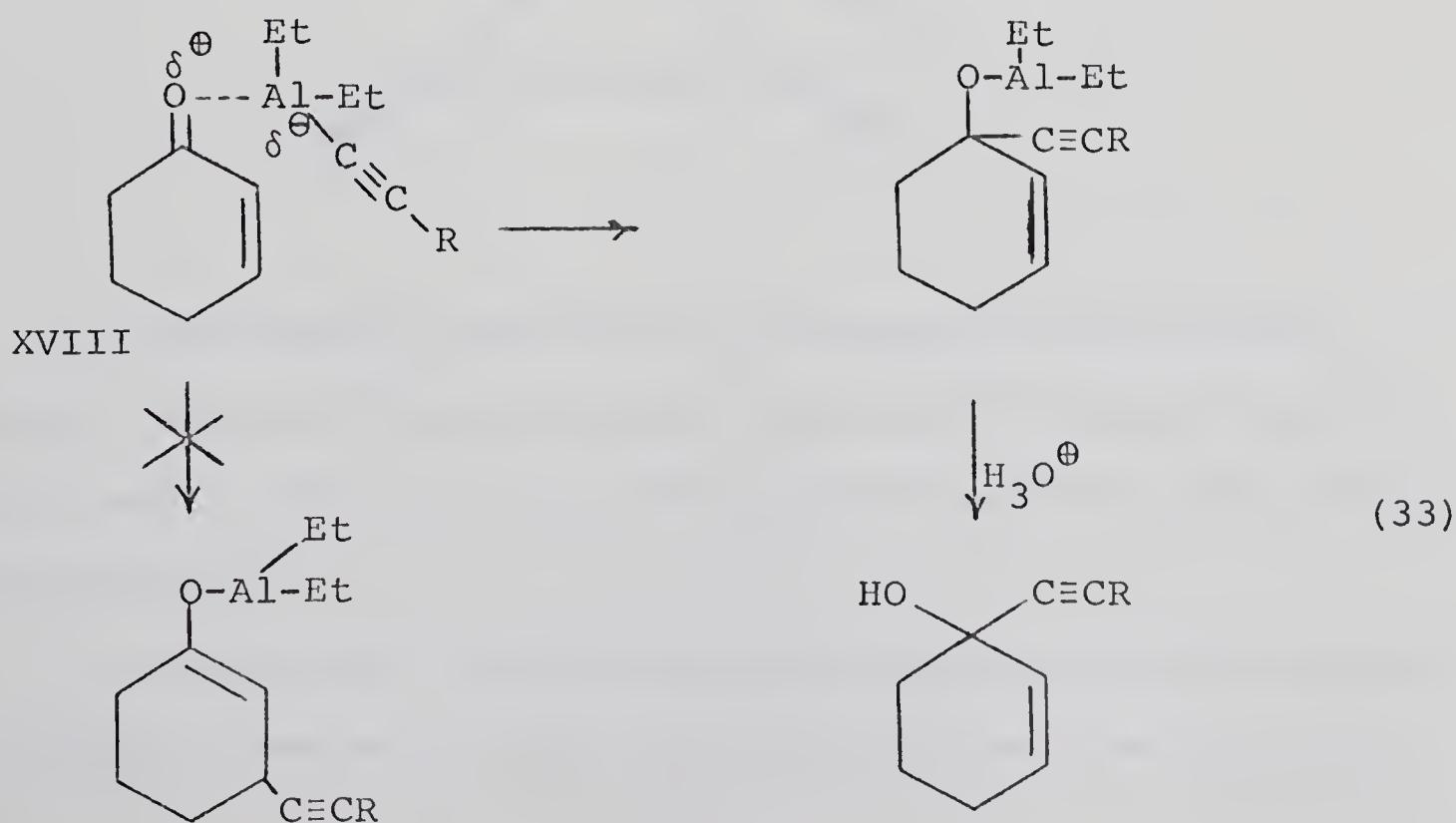




(32)

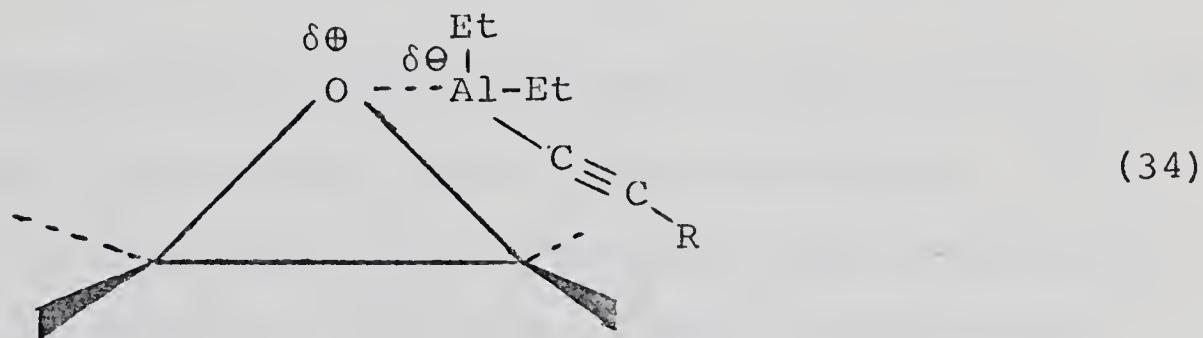


In cases involving enones locked in a transoid geometry (i.e. cyclic enones such as 2-cyclohexenone and isophorone) achievement of the six-centred transition state is impossible (XVIII) and hence conjugate addition is prohibited and 1,2-addition supervenes (eq. 33).





One condition which immediately becomes apparent from these considerations involves the ratio of aluminum reagent to enone substrate. If the 1,4-adduct arises from a six-centred transition state involving one molecule of enone and one molecule of alkynylalane then the yields of conjugate adduct should not be decreased if only a 1:1 ratio of alane to enone is employed. Two to one ratios of alane to enone had been employed by analogy to the epoxide opening work of Fried.<sup>32</sup> He reported reduced yields if less than this ratio was used. However, it is evident that opening of an epoxide by an alkynyl group attached to an aluminum atom (complexed with the epoxide oxygen) is not very favourable geometrically (*viz* eq. 34).



Consequently some sort of intermolecular process might be considered to supply the required alkynyl moiety but requirement for a greater amount of alane would not be unexpected.

To test the hypothesis regarding the necessary stoichiometry of enone to alane the reactions between the alane



and 1-acetylcyclohexene and benzalacetophenone, respectively, were repeated using only a 1:1 ratio of alane to enone. Thus, diethylhexynylalane was treated with an equimolar quantity of 1-acetylcyclohexene in a 15:1 ligroin:ether solvent system over 2.5 hr at 25°. Workup of the reaction mixture at this time yielded 68% of the conjugate adduct by glc. Similarly an equimolar quantity of benzalacetophenone was added to diethylphenylethylnylalane in a 12:1 ligroin:ether solvent system at room temperature. After 2 hr the reaction mixture was carefully hydrolysed and cooled. The precipitated crystals were collected and recrystallized to afford 85% of the conjugate adduct.

It thus appears obvious that no deleterious effect is introduced by employing only a 1:1 ratio of alane to enone substrate.

The sensitivity of this reaction to the nature of the solvent system has already been briefly considered. The use of THF in any appreciable quantities had a pronounced yield-reducing effect in the case of both 1-acetylcyclohexene and methyl vinyl ketone. In order to gain more information about this solvent dependency some reactions were done varying the ratio of ligroin:ether from the customary 10 to 15:1 value. When 1-acetylcyclohexene was reacted with 2 mole equivalents of diethylphenylethylnylalane in a 3:1 ether:ligroin solvent system a 94% yield of the conjugate adduct was obtained. This is a significant increase over



the 71% yield obtained previously in the 10:1 ligroin:ether system. As a result, the reactions that had given low yields in the 10:1 system were repeated in this new system to assess whether or not this yield increase was in fact a general phenomenon. However, pent-3-en-2-one afforded only 37% of the conjugate adduct (compared with 54% obtained previously) and 3-methylbut-3-en-2-one gave only 23% 1,4-addition (compared with 50% previously).

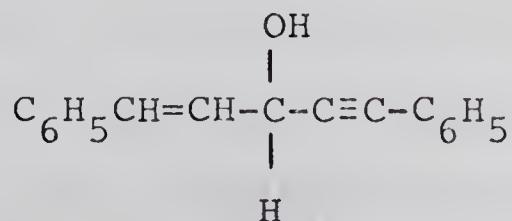
These results serve to emphasize the fact that for this reaction there seem to be no general set of reaction conditions (temperature, solvent etc) which will give optimal yields for all substrates. However, this is a common aspect of synthetic experience and recently the necessity of the proper choice of reaction variables in determining the success of various alkylation procedures (coupling and condensation processes) has been underlined.<sup>43-45</sup>

All reactions of the enone substrates had been conducted with the clear supernatant liquid decanted from the LiCl which precipitated during the formation of the alane reagent. This was done by analogy to previous experience<sup>32</sup> and involved experimentally a somewhat tedious filtration procedure under a nitrogen atmosphere. Whether or not the presence of LiCl during reaction was deleterious (and hence the filtration necessary) had not been determined. Consequently the reactions of benzalacetophenone, 1-acetyl-cyclohexene, mesityl oxide and methyl vinyl ketone with



the alane reagent were repeated omitting the decantation from the precipitated LiCl - the yields were found to be not significantly different from the cases where the reagent was decanted. As a result it would seem to be advisable to omit this somewhat tedious, time-consuming step.

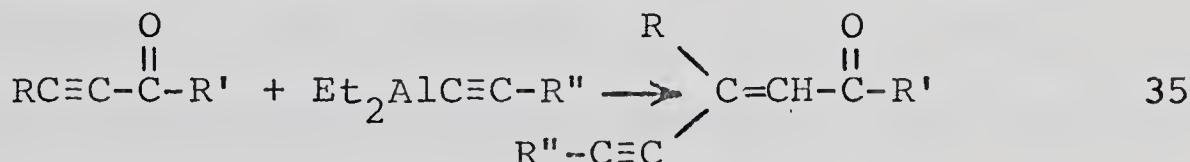
Having established the success of this method with acyclic  $\alpha,\beta$ -unsaturated ketones it was decided to briefly investigate the course of reaction with some other  $\alpha,\beta$ -unsaturated species. As a result, cinnamaldehyde was treated with diethylphenylethylnylalane at  $-30^\circ$ . Again the appearance of a yellowish-brown colour was noted on the addition of the aldehyde, but after stirring at  $-20^\circ$  for 1 hr the reaction mixture remained a deep amber. After carefully quenching the reaction in ice:concentrated HCl the pale yellow organic phase was worked up in the usual manner to afford a brown oil which exhibited no carbonyl absorption whatsoever in the infrared. Instead a broad hydroxyl absorption in the region  $3200-3500\text{ cm}^{-1}$  was noted. The crude oil was chromatographed on alumina. Elution with pentane:ether (1:1 by volume) and recrystallization from chloroform:pentane afforded the 1,2-adduct XIX in a 43% yield.





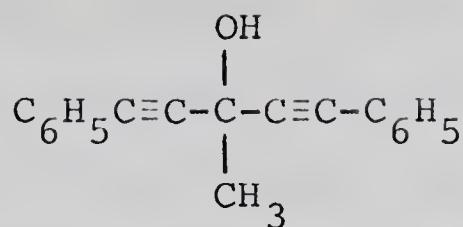
In the light of the fact that the best yields of the conjugate adducts were obtained for substrates possessing an aromatic moiety on the  $\beta$ -carbon, and that there was no evidence at all of any 1,4-addition in the case of cinnamaldehyde it would seem reasonable to conclude that  $\alpha,\beta$ -unsaturated aldehydes in general should only afford tertiary acetylenic carbonols with a dialkylalkynylalane reagent. No further examples were investigated.

A brief investigation of the course of the reaction of an alkynylalane with an  $\alpha,\beta$ -acetylenic ketone was undertaken. Conjugate addition of the acetylenic moiety to this type of compound would result in the formation of conjugated enynone systems (eq. 35).



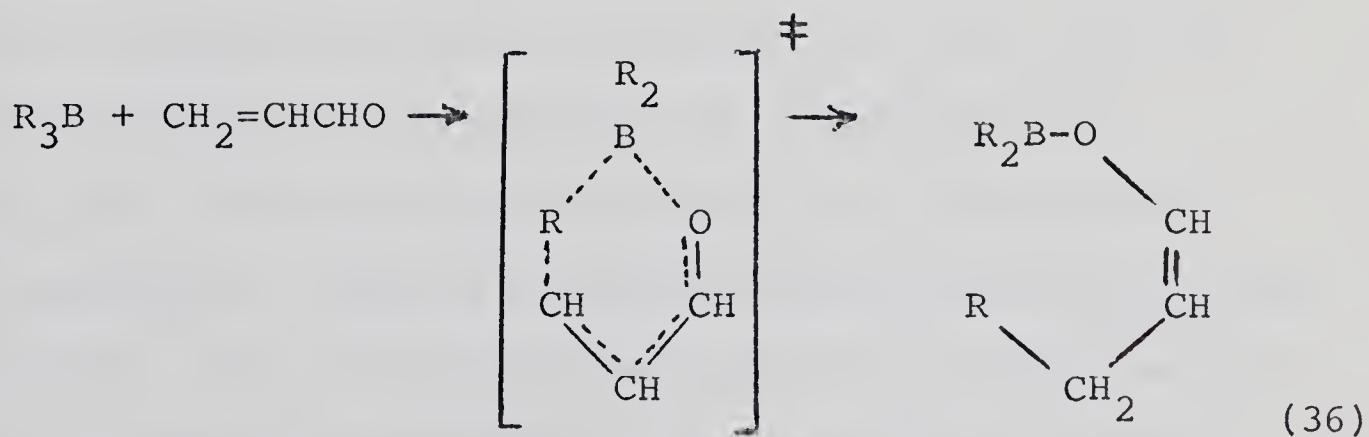
Consequently 4-phenyl-3-butyn-2-one was reacted with diethylphenylethylnylalane using conditions similar to those adopted for the enone-alane reaction. The crude product obtained on workup of the reaction showed no carbonyl absorption in the infrared but did exhibit a strong, broad absorption at  $3300 - 3500 \text{ cm}^{-1}$  indicative of intermolecularly bonded hydroxyl. The oil solidified on cooling, and after recrystallization afforded the 1,2-adduct, 1,5-diphenyl-3-methylpenta-1,4-diyn-3-ol (XX) in 60% yield.





XX

Brown and coworkers have established the ability of organoboranes to accomplish conjugate addition to  $\alpha,\beta$ -unsaturated carbonyl species such as methyl vinyl ketone,<sup>47</sup> acrolein,<sup>48</sup>  $\alpha$ -methylacrolein,<sup>49</sup>  $\alpha$ -bromoacrolein,<sup>49</sup> and 2-methylenecyclanones.<sup>49</sup> They observed the lack of reactivity of 2-cyclohexenone (analogous to the results observed here with the organoaluminum reagent) but also found that such substrates as *trans*-crotonaldehyde,, 1-acetylcyclohexene, and mesityl oxide failed to react as well. In spite of these latter observations it was hypothesized that the reaction was going through a six-centred cyclic transition state (eq. 36)



Recently,<sup>49</sup> however, these workers reported that the addition of as little as 5 mole percent of galvinoxyl (a known free radical scavenger) to the reaction mixture of, for example,



a trialkylborane with acrolein, caused complete inhibition of reaction. They concluded, therefore, that these conjugate addition reactions involve some radical chain process. In addition they report that trialkylboranes can be reacted with crotonaldehyde, ethylideneacetone and 2-cyclohexenone in the presence of free radical initiators such as acylperoxide,<sup>50</sup> light<sup>50</sup> and oxygen.<sup>51</sup> In the absence of these initiators these  $\alpha,\beta$ -unsaturated species are inert to organoboranes.

These observations suggested the possibility that some type of radical process might be associated with the mixed organoalane-enone reaction. Unfortunately, conducting the reactions in the presence of galvinoxyl produced conflicting results. Reaction of diethylphenylethyynylalane with 1-acetylcylohexene in the presence of 5 mole percent galvinoxyl caused a slight enhancement of the yield of 1,4-adduct to 94-96% from the 71-79% observed in the absence of scavenger. However, reaction of pent-3-en-2-one with the same alane reagent in the presence of 5 mole percent scavenger gave ~45% of conjugate adduct vs 54% obtained without scavenger. Clearly no conclusions can be drawn from these results. As a result it was decided to employ an experimental technique analogous to one which House used to discount the intermediacy of free radicals in the reaction of alkylcuprates with  $\alpha,\beta$ -unsaturated ketones.<sup>15</sup> By performing the conjugate addition reactions in the presence of



a readily-polymerizable monomer (isoprene) and detecting no polymerization of this monomer, House concluded that there could be no radical species present during the course of the reaction.

Styrene was chosen as the polymerizable monomer in this study. Determination of the concentration of styrene present at any time in the reaction mixture was done by quantitative ultraviolet spectroscopy. A blank run was performed to show that styrene monomer was stable to the workup conditions. Styrene was stirred with a solution of diethylhexynylalane for 2.5 hr, then the mixture was worked up in the usual manner. Examination of the residue by ultraviolet spectroscopy showed quantitative recovery of styrene. The reaction of diethylhexynylalane with 1-acetylcyclohexene was then repeated using identical conditions as before except that styrene monomer was present. Following the prescribed reaction period the solution was worked up in the usual fashion and the quantity of styrene monomer present was determined by ultraviolet spectroscopy as 100%. Glc investigation of the residue showed a 79% yield of 2-(hexynyl)acetylcyclohexane. Thus the conjugate addition reaction had proceeded as before without polymerizing the styrene. Next the reaction of pent-3-en-2-one with diethylphenylethylnylalane was repeated in the presence of styrene. After reacting for the prescribed period of time under



conditions identical to those used before, the reaction was worked up and again the quantity of styrene present by ultraviolet spectroscopy was 100%. A glc investigation of the hydrolysed reaction mixture showed a yield of 42% of the conjugate adduct, 4-methyl-6-phenylhex-5-yn-2-one.

These results seem to indicate that there were no intermediates involved in the alane reaction that could polymerize styrene. The question remained, however, whether or not styrene could be polymerized by a known free radical reaction. In order to establish this fact we used as a "model" the reaction of a trialkylborane with methyl vinyl ketone performed in the presence of styrene. A blank experiment showed that styrene would not be polymerized by just the trialkylborane (a solution of tributylborane and styrene in THF was stirred for 3 hr and let stand overnight - the following day a quantitative u.v. determination showed 100% of the original styrene monomer present). With this fact established, then, methyl vinyl ketone was reacted with tri-*n*-butylborane in the presence of styrene using essentially identical conditions to those employed by Brown.<sup>50</sup> Upon completion of the reaction the amount of styrene present was estimated at 63% by u.v. A glc determination of the amount of 2-octanone present was 36% (plus 20% of another isomer probably due to the lack of purity of the butylborane). By concentrating the reaction mixture *in vacuo* at room temperature (to avoid thermal polymerization



of the styrene) and diluting the oil obtained with pentane, it was possible to precipitate a quantity of polystyrene. When the alane reaction mixtures were concentrated *in vacuo* and diluted with pentane no precipitate was observed. It would thus seem that styrene can be polymerized by certain trialkylborane reactions. The alane reaction, however, cannot involve a free radical chain process which will polymerize styrene. However, this investigation does not offer definitive proof that there is no free radical nature to the alane reaction.

In all the experiments performed with the dialkyl-alkynylalanes there was never any evidence of any 1,2- or 1,4- addition of the ethyl groups on the aluminum atom to the enone substrates. This observation serves to reinforce those of Zweifel <sup>33-35</sup> and Fried <sup>32</sup> who also only observed products related to the migration of the carbon "ligand" with the highest degree of s-character. (This is in marked contrast, however, to observations reported later in this thesis concerning the reaction of mixed alkylalkynylboranes with diazo substrates. When dibutylhexynylborane was reacted with ethyl diazoacetate the only products detected were those resulting from the migration of the butyl groups attached to boron).

Having examined the reaction of the dialkyalkynyl-alane reagent with α,β-unsaturated carbonyl species in some detail, attention was briefly turned to utilization



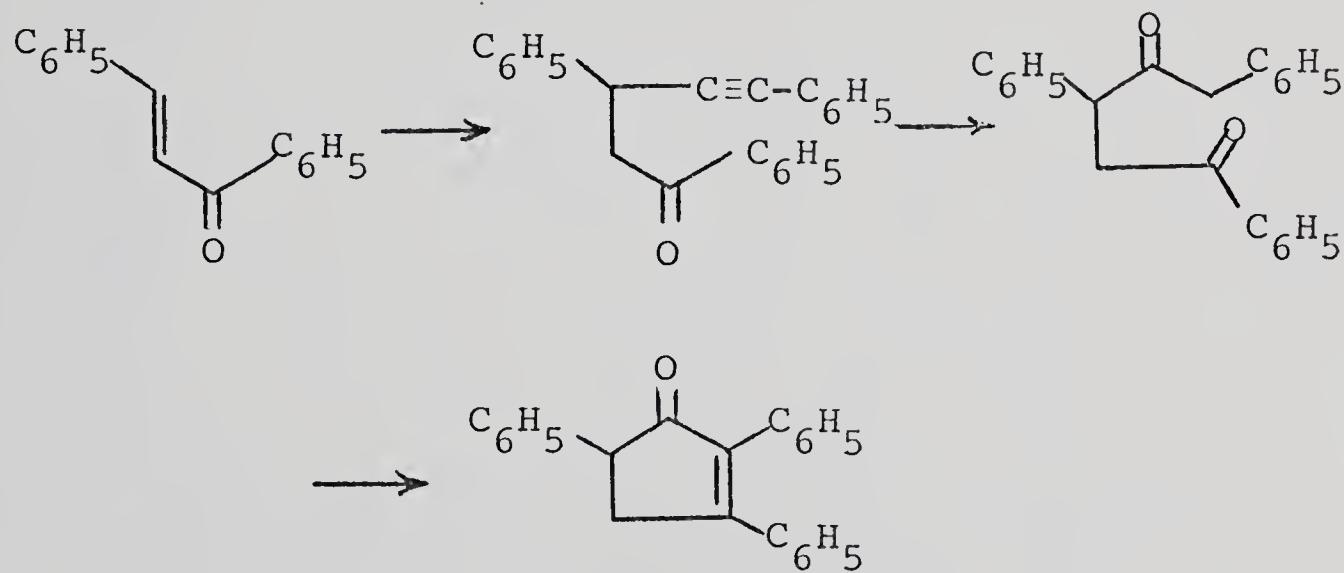
of the product of this reaction, the  $\gamma,\delta$ -acetylenic ketone. As mentioned previously, these ketones undergo specific hydration in good yield to afford the 1,4-diketone. The value of 1,4-diketones as synthetic intermediates leading to furans and pyrroles is well established.<sup>52,53</sup> In addition they provide cyclopentenone systems when cyclized in base. To illustrate the value of the  $\gamma,\delta$ -acetylenic ketones prepared above it was decided to convert one of these ketones to a substituted cyclopentenone system by specifically hydrating the triple bond and cyclizing the resultant 1,4-diketone.

The ketone chosen as starting material for this sequence was the conjugate adduct of phenylacetylene with benzalacetophenone, 1,3,5-triphenylpent-4-yn-1-one. This compound was obtained in good yield (81-85%) and was a stable crystalline solid. Attempts at hydration with 70% methanol using mercuric sulfate/sulfuric acid as catalyst resulted in quantitative recovery of starting material even after reflux for 5 hr. Use of more stringent hydration conditions (mercuric acetate, 90% acetic acid<sup>56</sup>) resulted in decomposition of the ynone to a resinous oil which exhibited no ir absorption in the carbonyl region. However, when the hydration was performed in 90% ethanol employing catalytic quantities of sulfuric acid and mercuric sulfate the starting ynone was hydrated to 1,3,5-triphenylpenta-1,4-dione in 95% yield. Cyclization of this diketone to the



cyclopentenone required fairly critical conditions. Stirring a quantity of the dione overnight with 2% alcoholic NaOH at 25° resulted in a gummy oil which showed no appreciable carbonyl absorption and contained at least four components by tlc. Refluxing the same mixture for only 1½ hr resulted, after workup and recrystallization, in the isolation of about 60% of the desired product, 2,3,5-triphenylcyclopent-2-en-1-one.

Consequently the overall yield in the conversion of benzalacetophenone to 2,3,5-triphenylcyclopent-2-en-1-one (as depicted in the scheme in eq. 37) was 46%.



If, however, the cyclization step was repeated under nitrogen an 85% yield of the final product was produced. This gave an overall yield of 65% of isolated, purified product.



The exclusion of oxygen from reactions involving enolate anions as intermediates (condensations, cyclizations, etc) has the beneficial effect of sharply reducing oxidative side reactions which would normally reduce the yield of the desired product.<sup>57</sup>



TABLE II

Reaction of Et<sub>2</sub>AlC≡CR with a Series of  $\alpha,\beta$ -unsaturated Ketones

R	Ketone	Rx'n Time (hr)	Solvent <sup>a</sup>	Product, % Yield
		& Temp °C	Ratio by Volume	
n-C <sub>4</sub> H <sub>9</sub>	1-acetylhexene	1, 25	E-L, 1:10	2-(1-hexynyl) acetylhexane, hexane, 85 <sup>b</sup>
n-C <sub>4</sub> H <sub>9</sub>	1-acetylclohexane	1.5, -15	E-L, 1:10	2-(1-hexynyl) acetylclohexane, hexane, 79 <sup>b</sup>
n-C <sub>4</sub> H <sub>9</sub>	methyl vinyl ketone	1.5, 1	E-L, 1:12	5-Decyn-2-one, 54 <sup>b</sup>
n-C <sub>4</sub> H <sub>9</sub>	methyl vinyl ketone	1, 25	E-L, 1:9	5-Decyn-2-one
C <sub>6</sub> H <sub>5</sub>	1-acetylhexene	1.25, -15	E-L, 1:10	2-(Phenylethylnyl) acetylhexane, 71 <sup>b</sup>
C <sub>6</sub> H <sub>5</sub>	benzalacetone	1.5, -10	E-L, 1:15	4,6-diphenylhex-5-yn-2-one 95 <sup>b</sup>
n-C <sub>4</sub> H <sub>9</sub>	benzalacetophenone	0.75, 5	E-L, 1:4	1,3-diphenylnon-4-yn-1-one 65 <sup>c</sup>
C <sub>6</sub> H <sub>5</sub>	benzalacetophenone	1.5, -15	E-L, 1:12	3-methyl-1-6-phenylhex-5-yn-2-one 50 <sup>b</sup>
C <sub>6</sub> H <sub>5</sub>	3-methylbut-3-en-2-one	1.5, -15	E-L, 1:12	3-methyl-1-6-phenylhex-5-yn-2-one 50 <sup>b</sup>
C <sub>6</sub> H <sub>5</sub>	pent-3-en-2-one	1, -10	E-L, 1:12	4-methyl-1-6-phenylhex-5-yn-2-one 54 <sup>b</sup>
n-C <sub>4</sub> H <sub>9</sub>	mesityl oxide	4, 25	E-L, 1:10	4,4-dimethyldec-5-yn-2-one 30 <sup>b</sup>
n-C <sub>4</sub> H <sub>9</sub>	cyclohex-2-en-1-one	3.5, 25	E-L, 1:16	d
n-C <sub>4</sub> H <sub>9</sub>	isophorone	22, 25	E-L, 1:9	d,e

(continued....)



- (a) E = ether, L = ligroin.
- (b) by vpc analysis
- (c) purified product isolated by distillation or crystallization
- (d) no C=O absorption in ir of crude reaction mixture
- (e) some starting material remaining.



TABLE III

1,2- vs 1,4- Addition in the Case of Some  $\alpha$ , $\beta$ -Unsaturated Ketones

R	Ketone	% 1,4-adduct <sup>a</sup>	% 1,2-adduct <sup>a</sup>	% 1,2-adduct + other products accounted for
n-C <sub>4</sub> H <sub>9</sub>	methyl vinyl ketone	48	8	56
C <sub>6</sub> H <sub>5</sub>	3-methylbut-3-en-2-one	50	38	88
C <sub>6</sub> H <sub>5</sub>	pent-3-en-2-one	54	11	65
n-C <sub>4</sub> H <sub>9</sub>	cyclohex-2-en-1-one	nil	76	76
n-C <sub>4</sub> H <sub>9</sub>	isophorone	nil	83 <sup>b</sup>	93
n-C <sub>4</sub> H <sub>9</sub>	mesityl oxide	30	40	70

(a) by glc

(b) plus 10% starting enone unreacted.



EXPERIMENTALGeneral Considerations

Ultraviolet (uv) spectra were determined using a Perkin-Elmer Ultraviolet Spectrophotometer Model 202.

Infrared (ir) spectra were recorded using a Perkin-Elmer 337G, Perkin-Elmer 421G or Unicam SP 1000 Infrared Spectrophotometer.

Nuclear magnetic resonance (nmr) spectra were recorded on a Varian A-60 or HR-100 Spectrometer. Unless otherwise stated deuteriochloroform ( $\text{CDCl}_3$ ) was employed as the solvent with tetramethylsilane (TMS) as the internal reference. Chemical shifts are reported as  $\tau$  values relative to TMS = 10. The following abbreviations are used in the text: s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet.

Mass spectra were recorded on an AEI Model MS-2 or Model MS-9 Spectrometer. Spectra are recorded in the following fashion: m/e:peak mass (relative intensity).

Gas liquid chromatography (glc) was performed using an Aerograph A-90-P3 and a Varian Aerograph Series 1200 chromatograph.

Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected.

Refractive indices were measured on a Bausch and Lomb Abbé -3L Refractometer.



Ligroin, bp 63-75°, supplied by Eastman Kodak Co., was successively treated with KMnO<sub>4</sub>, conc. H<sub>2</sub>SO<sub>4</sub>, KMnO<sub>4</sub>, H<sub>2</sub>O, then refluxed over CaH<sub>2</sub> and distilled from CaH<sub>2</sub> prior to use.

Reaction of Dihexynylcopperlithium with Methyl Vinyl Ketone

To a solution of 1-hexyne (13.2 ml; 120 mmole) in THF (60 ml) was slowly added a solution of *n*-butyllithium in hexane <sup>21</sup> (120 mmole) at 0° under dry nitrogen. The resultant solution was cooled to -78° and purified <sup>20</sup> cuprous iodide (11.4 g; 60 mmole) was added in small portions. The resultant heterogeneous mixture was stirred at -78° for 2 hr and then a solution of methyl vinyl ketone (2.1 g; 30 mmole) in THF (20 ml) was slowly added (2 hr). After stirring an additional 0.5 hr an aliquot was withdrawn and hydrolysed in dilute HCl (3 N), dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated. Examination by infrared spectroscopy showed no carbonyl absorption but a large amount of hydroxyl absorption at 3500 cm<sup>-1</sup>. The remainder of the reaction mixture was poured into dilute HCl and filtered. The organic phase was separated and the aqueous layer was extracted with ether (3 x 25 ml). The combined organic extracts were dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated. Examination of the residue by glc (5% SE30: 155°) showed a negligible amount of the 1,4-adduct, 5-decyn-2-one. Upon distillation 2.8 g (62%) 3-methylnon-1-en-4-yn-ol (XV) was isolated as



a colourless liquid, bp 90-91° (7 mm),  $n_D^{25}$  1.4545; ir (thin film) 3200, 3500 (OH), 3100, 1645, 930 (CH=CH<sub>2</sub>) 2250 cm<sup>-1</sup> (C≡C); nmr: τ 3.75 - 5.15 (m, 3) CH=CH<sub>2</sub>, 7.29 (s, 1) -OH, 7.81 (t, 2) C≡C-CH<sub>2</sub>-CH<sub>2</sub>, 8.51 (s, 3) CH<sub>3</sub>-OH, 8.55 (m, 4) CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>3</sub>, 9.10 (t, 3) CH<sub>3</sub>-CH<sub>2</sub>-; mass spectrum m/e: 152(14), 137(50), 109(70), 95(26), 81(20), 77(14), 67(32), 55(37), 43(100), 39(26). Anal. Calcd. for C<sub>10</sub>H<sub>16</sub>O: C, 78.90; H, 10.59. Found: C, 78.98; H, 10.69.

#### Typical Preparation of a Dialkylalkynylalane:

All operations were carried out under a dry nitrogen atmosphere. To a solution of alkyne (80 mmole) dissolved in dry, olefin-free ligroin (50 ml) was slowly added a solution of *n*-butyllithium in hexane<sup>21</sup> maintaining the temperature below ca 15°. After stirring the resultant suspension for 15 min at 20°, 15 ml of dry ether was added. Then a solution of diethylaluminum chloride<sup>21</sup> (10 ml; 80 mmole) in ligroin (20 ml) was added to the cooled (~15°) suspension followed by an additional 60 ml of ligroin. The reaction mixture was then stirred for 0.5 hr at ~25°. Depending upon the experimental procedure being followed, the crude mixture containing the diethylalkynylalane was either used at this point, or alternatively, the LiCl was allowed to settle and the clear supernatant was decanted under nitrogen and then used. The ratio of ligroin to ether in the solution of the dialkylalkynylalane ranged



from 10 to 15:1.

Typical Workup Procedure for Dialkylalkynylalane-Enone Reactions.

Unless otherwise stated the following procedure was adopted for the workup of the reactions of the dialkylalkynyl-alane with various  $\alpha,\beta$ -unsaturated ketones.

After stirring for the prescribed period of time the reaction mixture of alane and enone was carefully poured, in small portions, into a stirred mixture of ice: concentrated HCl (approximately 1:1 by weight). The mixture was stirred until the gas evolution subsided and then the two layers were separated and the aqueous phase was extracted with ether (3 x 40 ml). The combined organic phase was washed carefully with saturated bicarbonate, water, and finally dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated to afford a crude, oily residue.

The reaction of Diethylhexynylalane with 1-Acetylcyclohexene at 25°.

To a solution of 1-hexyne (8.8 ml; 80 mmole) in dry olefin-free ligroin (100 ml) was added a solution of *n*-butyllithium in hexane<sup>21</sup> (80 mmole) maintaining the temperature below 15°. After stirring the resultant thick, gelatinous mixture for 15 min at this temperature, a solution of diethylaluminum chloride<sup>21</sup> (10 ml; 80 mmole)



in ligroin (15 ml) was slowly added. Stirring this mixture for 2 hr produced no noticeable change in appearance. Consequently ether (17 ml) was added all at once. An exothermic reaction immediately ensued which caused the temperature of the reaction to rise by 10 to 15°. The stirrer was stopped after 15 min and a finely divided, white, crystalline precipitate settled out to leave a clear, colourless supernatant. The supernatant was decanted under nitrogen and a solution of 1-acetylcyclohexene (4.96 g; 40 mmole) in ligroin (20 ml) was slowly added. Contact of the enone solution with the alane solution caused the appearance of a yellowish tinge which rapidly disappeared at first but faintly persisted upon completion of the addition. After stirring for 1 hr the reaction mixture was worked up as described above. The yield of 2-(1-hexynyl)acetylcyclohexane in the yellow oil so obtained was 85% by glc (5% SE30; 150°). A sample of the compound was collected by preparative glc (5% SE30; 180°): ir (thin film)  $1710\text{ cm}^{-1}$  ( $\text{C=O}$ ); nmr:  $\tau$  7.75 (m, 2)  $\text{C}\equiv\text{CCH}_2-\text{CH}_2$ , 7.82 (s, 3)  $\text{CH}_3-\text{C=O}$ , 7.90 - 8.90 (broad m, 14)  $\text{CH}_2$ , 9.10 (t, 3)  $\text{CH}_3-\text{CH}_2$ ; mass spectrum:  $m/e$  206(10), 188(55), 173(15), 163(100), 149(30), 145(35) 131(42), 91(40), 43(60). Anal. Calcd. for  $\text{C}_{14}\text{H}_{22}\text{O}$ : C, 81.50; H, 10.75. Found: C, 81.59; H, 10.59.



Reaction of Diethylhexynylalane with 1-Acetylhexene at Low Temperature.

A solution of diethylhexynylalane (40 mmole) was prepared as described previously in an approximately 10:1 ligroin:ether solvent system. After being decanted from the precipitated LiCl the supernatant was cooled to -15° and a solution of 1-acetylhexene (2.48 g; 20 mmole) in ligroin (20 ml) was slowly added (0.75 hr). The resultant slightly yellow solution was stirred an additional 0.75 hr at which time hydrolysis and examination of an aliquot by infrared spectroscopy showed complete disappearance of starting material (no carbonyl band at 1680  $\text{cm}^{-1}$ ). The remainder of the reaction mixture was worked up as described above and the yield of 2-(1-hexynyl)acetylhexane in the crude residue was determined as 79% by glc (5% SE30; 150°). A sample was collected by preparative glc (5% SE30; 180°) and proved to be identical in all respects to the product obtained from the above reaction.

Reaction of Diethylhexynylalane with Methyl Vinyl Ketone at 0°.

A solution of diethylhexynylalane (80 mmole) in a solvent mixture of 12:1 ligroin:ether was prepared as described previously. The clear supernatant was decanted from the precipitated LiCl and cooled to ~0°. A solution of methyl vinyl ketone (2.8 g; 40 mmole) in ligroin



(15 ml) was then added slowly (0.5 hr) and the resultant pale yellow solution was stirred for 1 hr. Hydrolysis of an aliquot at this point and examination by infrared spectroscopy indicated complete consumption of starting material (no C=O absorption at  $1680\text{ cm}^{-1}$ ). The remainder of the reaction mixture was worked up as described above. The yield of 5-decyn-2-one was 48% by glc (5% SE30:  $110^\circ$ ). A sample of this ketone was collected by preparative glc (10% SE30;  $165^\circ$ ) and exhibited: ir (thin film)  $1710\text{ cm}^{-1}$  (C=O); nmr:  $\tau$  7.45 (m,4)  $\text{CH}_2-\text{C}\equiv\text{C}$ ,  $\text{CH}_2-\text{C=O}$ , 7.81 (s,3)  $\text{CH}_3\text{C=O}$ , 7.83 (m,2)  $\text{CH}_2-\text{CH}_2-\text{C}\equiv\text{C}$ , 8.55 (m,4)  $\text{CH}_3\text{CH}_2\text{CH}_2$ , 9.08 (t,3)  $\text{CH}_3-\text{CH}_2-$ ; mass spectrum:  $m/e$  152(.6), 137(1.5), 109(36), 95(11), 81(13), 67(22), 43(100). Anal. Calcd. for  $\text{C}_{10}\text{H}_{16}\text{O}$ : C, 78.90; H, 10.59. Found: C, 78.94; H, 10.63.

The yield of the 1,2-adduct, 3-methylnon-1-en-4-yn-3-ol (XV) was determined as 8% by glc (5% SE30;  $110^\circ$ ). A sample was isolated by preparative glc (5% SE30;  $100^\circ$ ) and proved to be identical with XV obtained above.

Reaction of Diethylhexynylalane with Methyl Vinyl Ketone at Room Temperature.

A solution of diethylhexynylalane (80 mmole) in a solvent mixture of 9:1 ligroin:ether was prepared as described above. The clear supernatant was decanted from the precipitated LiCl and a solution of methyl vinyl ketone (2.8 g; 40 mmole) in ligroin (15 ml) was then slowly added at



25°. After 1 hr, hydrolysis of an aliquot and examination by infrared spectroscopy showed no carbonyl absorption at  $1680\text{ cm}^{-1}$  (starting material carbonyl); the remainder of the reaction mixture was worked up as described above. Examination of the residue by glc (5% SE30; 85°) indicated a yield of 54% of the conjugate adduct, 5-decyn-2-one. A sample was collected by preparative glc (10% SE30; 165°) and proved to be identical with the product obtained from the above reaction.

The Reaction of Diethylphenylethylnylalane with 1-Acetylcylohexene.

A solution of diethylphenylethylnylalane (80 mmole) in a solvent mixture of 10:1 ligroin:ether was prepared as previous described. The clear supernatant was decanted from the precipitated LiCl and cooled to -15°. A solution of 1-acetylcylohexene (4.96 g; 40 mmole) in ligroin (20 ml) was then added slowly (1 hr). After stirring an additional 0.5 hr an aliquot was hydrolysed. Examination by infrared spectroscopy showed complete consumption of starting material. The remainder of the reaction mixture was worked up as described above and the yield of the 1,4-adduct, 2-(phenyl-ethynyl)acetylcylohexane was determined as 71% by glc (5% SE30; 240°). A portion of the crude residue was subjected to vacuum distillation through a spinning band column and the conjugate adduct was collected; bp 154-155° (1.8 mm)



$n_D^{21} = 1.5904$ . ir (liquid film) 1720 (C=O), 1601, 1500, 760, 700  $\text{cm}^{-1}$   $\text{C}_6\text{H}_5$ ; nmr:  $\tau$  2.70 (m,5)  $\text{C}_6\text{H}_5$ , 7.21 - 9.10 (broad m, 10)  $\text{CH}_2$ , 7.79 (s,3)  $\text{CH}_3\text{C=O}$ . Mass spectrum (calcd. for  $\text{C}_{16}\text{H}_{18}\text{O}$  226.1358; found 226.1361):  $m/e$  226(55), 211(42), 208(100), 197(40), 178(30), 115(45), 91(30), 43(45). Anal. Calcd. for  $\text{C}_{16}\text{H}_{18}\text{O}$ : C, 84.91; H, 8.02. Found: C, 84.61; H, 7.74.

Reaction of Diethylhexynylalane with Methyl Vinyl Ketone at -78° in the Presence of THF.

Diethylhexynylalane (80 mmole) in a solvent mixture of 1:1.5 THF:ligroin was prepared as described previously. The clear supernatant was decanted from the precipitated LiCl and cooled to -78°. Methyl vinyl ketone (2.80 g; 40 mmole) in THF (30 ml) was then slowly added (0.5 hr). After a further 1.25 hr the reaction was worked up as described above. Examination of the crude reaction mixture by glc (5% SE30; 70°) showed ~70% methyl vinyl ketone present. No trace of the conjugate adduct 5-decyn-2-one was detected.

Reaction of Diethylhexynylalane with Methyl Vinyl Ketone at 0° in THF.

Diethylhexynylalane (50 mmole) in a solvent mixture of 1:1 ligroin:THF was prepared as described at the beginning of this experimental section. The clear supernatant was decanted from the precipitated LiCl under  $\text{N}_2$  and cooled to 0°. Methyl vinyl ketone (1.75 g; 25 mmole) in THF (30 ml) was added slowly to this solution (0.5 hr). After stirring at



this temperature for 2 hr the reaction mixture was warmed to 25° and worked up as described above. The residue showed no trace of starting material by glc but also there was only a negligible amount of the 1,4-adduct, 5-decyn-2-one.

Reaction of Diethylphenylethylnylalane with 1-Acetylcyclohexene at 0° in THF.

Diethylphenylethylnylalane (30 mmole) in a solvent mixture of 3:1 THF:ligroin was prepared as previously described. After decantation from the precipitated LiCl under N<sub>2</sub> the clear supernatant was cooled to 0° and 1-acetylcyclohexene (1.86 g; 15 mmole) in THF (15 ml) was slowly added. After stirring for 1.25 hr hydrolysis of an aliquot and examination by infrared spectroscopy showed considerable hydroxyl absorption at 3500 cm<sup>-1</sup>, but complete absence of starting enone. The remainder of the reaction mixture was worked up as described above and glc examination (5% SE30; 230°) of the residue indicated 3% of the conjugate adduct 2-(phenylethynyl)acetylcyclohexane.

Reaction of Benzalacetophenone with Diethylphenylethylnylalane.

Diethylphenylethylnylalane (80 mmole) in a solvent system of 10:1 ligroin:ether was prepared as described above, and after decantation from the precipitated LiCl the clear supernatant was treated with benzalacetophenone (8.32 g; 40 mmole) in 15 ml 3:1 ether:ligroin. The mixture was stirred



for 4 hr. At this point hydrolysis of an aliquot and examination by infrared spectroscopy indicated complete consumption of starting material. The reaction mixture was hydrolysed by carefully pouring into ice:concentrated HCl. The organic phase was allowed to stand in the refrigerator overnight. The white crystals were collected and recrystallized from benzene:pentane (1:3 by volume) to afford 10 g (81%) of white crystals of 1,3,5-triphenylpent-4-yn-1-one, mp 93.5 - 94.5°: ir (CHCl<sub>3</sub>) 1685 (C=O), 1598, 1490, 1450, 700 cm<sup>-1</sup> (C<sub>6</sub>H<sub>5</sub>); nmr: τ 6.45 (m,2), C=OCH<sub>2</sub>-CH, 5.30 (t,1) CH-CH<sub>2</sub>, 1.99 - 2.95 (m,15) C<sub>6</sub>H<sub>5</sub> x3; mass spectrum (calcd. for C<sub>23</sub>H<sub>18</sub>O: 310.1358; found 310.1351) m/e 310(40), 233(17), 205(100), 191(45), 105(72), 77(55), 51(13). Anal. Calcd. for C<sub>23</sub>H<sub>18</sub>O: C, 89.00; H, 5.85. Found: C, 88.78; H, 6.06.

Reaction of Diethylhexynylalane with Benzalacetophenone:

Diethylhexynylalane (40 mmole) was prepared as described at the beginning of this experimental section in a 1:4 ether:ligroin solvent system. After decantation from the precipitated LiCl, the clear supernatant was cooled to 5°. Benzalacetophenone (4.16 g; 20 mmole) in 40 ml 3:1 ether:ligroin was then added slowly (0.5 hr). After stirring an additional 15 min, hydrolysis and examination of an aliquot by infrared spectroscopy indicated complete consumption of starting material. There was also a negligible amount of hydroxyl absorption evident. The remainder of the



reaction mixture was worked up as described above and the crude, oily product was subjected to distillation. This afforded 3.8 g (65%) of 1,4-adduct, 1,3-diphenyl-non-4-yn-1-one, bp 175 - 180° (50 μ),  $n_D^{25}$  1.5600 ir (liquid film): 1680 (C=O), 1590, 1480, 1450, 750, 690  $\text{cm}^{-1}$  ( $\text{C}_6\text{H}_5$ ); nmr: τ 2.0 - 2.9 (m, 10)  $\text{C}_6\text{H}_5 \times 2$ , 5.61 (m, 1)  $\text{CH}-\text{CH}_2$ , 6.70 (m, 2)  $\text{C}=\text{OCH}_2-\text{CH}$ , 7.9 (m, 2)  $\text{CH}_2-\text{C}\equiv\text{C}$ , 8.68 (m, 4)  $\text{CH}_3-\text{CH}_2-\text{CH}_2$ , 9.15 (t, 3)  $\text{CH}_3-\text{CH}_2$ . Mass spectrum (calcd. for  $\text{C}_{21}\text{H}_{22}\text{O}$ : 290.1671; Found: 290.1666)  $m/e$  290(14), 247(38), 233(61), 170(18), 129(19), 115(18), 105(100), 91(32), 77(60), 51(15).

#### Reaction Between Benzalacetone and Diethylphenylethylnylalane.

Diethylphenylethylnylalane (80 mmole) in a 15:1 ligroin:ether solvent system was prepared as previously described, and after decantation from the precipitated LiCl, the clear supernatant was cooled to -10°. Benzalacetone (4.84 g; 40 mmole) in 40 ml 6:1 ligroin:ether was added slowly and after stirring for 1.5 hr hydrolysis of an aliquot and examination by infrared spectroscopy indicated complete consumption of starting enone. There was also negligible hydroxyl absorption present. The remainder of the reaction mixture was worked up as described above and the yield of 4,6-diphenylhex-5-yn-2-one in the crude reaction mixture was estimated as 95% by glc (5% SE30; 200°). The crude yellow oil was chromatographed over neutral (Woelm) alumina (Activity III).



Elution with benzene gave 7 g (71%) of the 1,4-adduct, ir (CHCl<sub>3</sub>): 1720 (C=O), 1600, 1480, 690 cm<sup>-1</sup> (C<sub>6</sub>H<sub>5</sub>) nmr:  $\tau$  2.72 (m,10) C<sub>6</sub>H<sub>5</sub>x2, 5.62 (t,1) CH-CH<sub>2</sub>, 7.16 (q,2) CH<sub>2</sub>-CH, 8.00 (s,3) CH<sub>3</sub>C=O, mass spectrum (calcd. for C<sub>18</sub>H<sub>16</sub>O: 248.1201; found: 248.1196) m/e 248(10), 233(20), 205(100), 191(45), 89(30), 165(16), 127(19), 78(37), 77(35), 51(35), 43(60). Anal. Calcd. for C<sub>18</sub>H<sub>16</sub>O: C, 87.06; H, 6.49. Found: C, 86.76; H, 6.34.

Reaction of Diethylphenylethylnylalane with Methyl Isopropenyl Ketone.

Diethylphenylethylnylalane (80 mmole) in a 12:1 ligroin:ether solvent system was prepared as outlined at the beginning of this experimental section. After decantation from the precipitated LiCl under N<sub>2</sub> the clear supernatant was cooled to -15°. Methyl isopropenyl ketone (3.36 g; 40 mmole) was added slowly to the cold solution and after stirring for 1.5 hr hydrolysis of an aliquot and examination by infrared spectroscopy indicated complete consumption of starting enone. The remainder of the reaction mixture was worked up as described above and the yield of 3-methyl-6-phenylhex-5-yn-2-one in the yellow residue was estimated as 50% by glc (5% SE30; 150°). A sample was collected by preparative glc (5% SE30; 170°). ir (liquid film): 1710 (C=O), 1600, 1480, 760 cm<sup>-1</sup> (C<sub>6</sub>H<sub>5</sub>); nmr:  $\tau$  2.71 (m,5) C<sub>6</sub>H<sub>5</sub>, 7.48 (m,2) CH<sub>2</sub>-CH, 7.50 (m,1) CH-CH<sub>2</sub>, 7.91 (s,3) CH<sub>3</sub>C=O, 8.82 (d,3) CH<sub>3</sub>-CH,



mass spectrum (calcd. for  $C_{13}H_{14}O$ : 186.1045; found: 186.1050)  $m/e$  186(54), 171(100), 143(15), 141(13), 128(50), 115(52), 43(50). Anal. Calcd. for  $C_{13}H_{14}O$ : C, 83.83; H, 7.58. Found: C, 84.08; H, 7.66.

Reaction Between Pent-3-en-2-one and Diethylphenylethylnylalane

Diethylphenylethylnylalane (80 mmole) in a 12:1 ligroin:ether solvent system was prepared as described at the beginning of this experimental section. After decantation from the precipitated LiCl under  $N_2$  the clear supernatant was cooled to -15°. Pent-3-en-2-one (3.36 g; 40 mmole) in ligroin (20 ml) was slowly added to the above cooled solution and the resultant mixture stirred for 1 hr. Hydrolysis and examination of an aliquot at this time indicated complete consumption of starting material. The remaining reaction mixture was worked up as outlined above and glc examination (5% SE30; 150°) of the residue indicated a 54% yield of the 1,4-adduct, 4-methyl-6-phenylhex-5-yn-2-one. A sample was collected by preparative glc (10% SE30; 200°). ir ( $CHCl_3$ ) 1715 (C=O), 1600, 1490, 920  $cm^{-1}$  ( $C_6H_5$ ); nmr:  $\tau$  2.71 (m,5)  $C_6H_5$ , 6.85 (q,1)  $CH-CH_3$ , 7.42 (q,2)  $C-CH_2-C-H$ , 7.89 (s,3)  $CH_3-C=O$ , 8.76 (d,3)  $CH_3-CH$ ; mass spectrum (calcd. for  $C_{13}H_{14}O$ : 186.1045; found: 186.1051)  $m/e$  186(10), 171(100), 143(34), 129(25), 128(68), 115(20), 77(20), 63(10), 51(14), 43(60). Anal. Calcd. for  $C_{13}H_{14}O$ : C, 83.83; H, 7.58. Found: C, 84.08; H, 7.55.



Preparation of the 1,2-Adduct of 1-Hexyne and 2-Cyclohexen-1-one.

A solution of 1-hexyne (70 mmole) in THF (30 ml) was treated with a solution of *n*-butyllithium in hexane<sup>21</sup> (70 mmole) at 0°. 2-Cyclohexenone (5.76 g; 60 mmole) in THF (15 ml) was slowly added to the above solution (35 min) maintaining the temperature at 0°. The solution was then allowed to warm to 25°, stirred at this temperature for 0.5 hr and then refluxed for 0.5 hr. The reaction mixture was then poured into saturated NH<sub>4</sub>Cl and stirred for 15 min. The two layers were separated and the aqueous phase was extracted with ether (2 x 30 ml). The combined organic extract was dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated to leave a pale yellow oil. This was subjected to distillation and afforded 8 g (75%) 1-(1-hexynyl)cyclohex-2-en-1-ol, bp 103-105 (4mm), *n*<sub>D</sub><sup>25</sup> 1.4936. ir (CHCl<sub>3</sub>) 3600 cm<sup>-1</sup> (nonbonded OH); nmr: τ 4.25 (s,2) CH=CH, 7.41 (s,1) -OH, 7.60 - 8.30 (m,8) CH<sub>2</sub>, 8.3-8.8 (m,4) CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub> 9.1 (t,3) CH<sub>3</sub>-CH<sub>2</sub>; mass spectrum (calcd. for C<sub>12</sub>H<sub>18</sub>O: 178.1358; found 178.1355) m/e 178(.6), 160(100), 145(23), 131(25), 167(73), 165(55), 91(66), 18(85). Anal. Calcd. for C<sub>12</sub>H<sub>18</sub>O: C, 80.85; H, 10.18. Found: C, 80.95; H, 9.95.

Preparation of the 1,2-Adduct of 1-Hexyne and Isophorone.

A solution of 1-hexyne (80 mmole) in THF (50 ml) was treated with a solution of *n*-butyllithium in hexane<sup>21</sup> (80



mmole) at 5°. Isophorone (8.28 g; 60 mmole) in THF (20 ml) was slowly added to the above solution and after stirring for 0.75 hr the solution was allowed to warm to 25°. After stirring at this temperature for 1 hr the solution was refluxed for 1.5 hr, cooled, and poured into saturated NH<sub>4</sub>Cl. The two layers were separated and the aqueous phase was extracted with ether (2 x 30 ml). The combined organic phase was dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated. The crude residue was subjected to distillation and afforded 9 g (68%) 1-(1-hexynyl)-3,5,5-trimethylcyclohex-2-en-ol, bp 123 - 124° (3 mm),  $n_D^{26} = 1.4850$ . ir (liquid film): 3150 - 3500 (OH), 2220 (C≡C), 1670 cm<sup>-1</sup> (C=C); nmr: τ 4.55 (m,1) C=C, 7.72 (broad s, 1) OH, 7.78 (t,2) CH<sub>2</sub>-CH<sub>2</sub>C≡C, 8.35 - 8.80 (m,4) CH<sub>2</sub>-CH<sub>2</sub>, 8.28 (s,3) CH<sub>3</sub>-C=, 8.9 (s,6) CH<sub>3</sub>-CCH<sub>3</sub>, 8.15 (s,2) CH<sub>2</sub>, 8.25 (s,2) CH<sub>2</sub>, 9.15 (t,3), CH<sub>3</sub>-CH<sub>2</sub>; mass spectrum m/e 220(15), 202(100), 187(85), 159(20), 145(47), 131(35), 119(40), 105(23), 91(28), 81(21), 41(26), 18(65). Anal. Calcd. for C<sub>15</sub>H<sub>24</sub>O: C, 81.76; H, 10.98. Found: C, 82.05; H, 10.96.

#### Preparation of the 1,2-Adduct of Mesityl Oxide and 1-Hexyne.

A solution of 1-hexyne (80 mmole) in THF (50 ml) was treated with a solution of *n*-butyllithium in hexane <sup>21</sup> (80 mmole) at 0°. Mesityl oxide (5.88 g; 60 mmole) in THF (20 ml) was slowly added to the resultant solution. Upon completion of the addition (0.5 hr) the solution was warmed



to 25° and then refluxed for 5 hr. The reaction mixture was then cooled to 25° and poured into saturated NH<sub>4</sub>Cl and the two layers were separated. The aqueous phase was extracted with ether (2 x 30 ml) and the combined extract was dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated. The crude residue was subjected to distillation and afforded 7.6 g (70%) 2,4-di-methyldec-5-yn-2-en-4-ol, bp 78 - 80° (3.5 mm),  $n_D^{25} = 1.4658$ . ir (liquid film) 3150 - 3500 (OH), 2120 (C≡C), 1665 cm<sup>-1</sup> (C=C); nmr: τ 4.61 (m,1) CH=C, 7.39 (s,1) OH, 7.80 (t,2) CH<sub>2</sub>CH<sub>2</sub>-C≡C, 8.10 (d,3) CH<sub>3</sub>C=CH, 8.29 (d,3) CH<sub>3</sub>C=CH, 8.45 (s,3) CH<sub>3</sub>C-OH, 8.29 - 8.75 (m,4) CH<sub>3</sub>-CH<sub>2</sub>C<sub>2</sub>, 9.10 (t,3) CH<sub>3</sub>CH<sub>2</sub>; mass spectrum (calcd. for C<sub>20</sub>H<sub>12</sub>O: 180.1514; found: 180.1511) m/e 180(.7), 162(40), 149(20), 133(90), 120(48), 119(45), 118(55), 105(100), 91(63), 79(26), 77(31), 65(16), 18(70). Anal. Calcd. for C<sub>12</sub>H<sub>20</sub>O: C, 79.94; H, 11.18. Found: C, 80.03; H, 10.91.

#### Reaction of Diethylhexynylalane with 2-Cyclohexenone.

Diethylhexynylalane (80 mmole) in a 16:1 ligroin:ether solvent system was synthesized as described at the beginning of this experimental section. The clear supernatant was decanted from the precipitated LiCl under nitrogen and 2-cyclohexenone (3.8 g; 40 mmole) in ligroin (40 ml) was added slowly at room temperature (25°). After stirring for 3.5 hr the reaction mixture was worked up using the general workup procedure described above. The residue so obtained was



examined by infrared spectroscopy and showed no carbonyl absorption. There was, however, considerable hydroxyl absorption present at  $3100 - 3500 \text{ cm}^{-1}$ . The yield of 1-(1-hexynyl)cyclohex-2-en-1-ol in the residue was determined as 76% by glc (10% SE30;  $170^\circ$ ). A sample was collected by preparative glc (10% SF30:  $140^\circ$ ) and proved to be identical with the compound prepared on pg 79.

Reaction of Diethylhexynylalane with Isophorone.

Diethylhexynylalane (60 mmole) in a 9:1 ligroin:ether solvent system was prepared as outlined at the beginning of this experimental section. After decantation, the clear supernatant was treated with isophorone (4.14 g; 30 mmole) in ligroin (20 ml). The resultant mixture was stirred for 22 hr and then worked up as described above. The infrared of the crude, oily product showed some carbonyl absorption at  $1680 \text{ cm}^{-1}$  (starting enone) and a large hydroxyl absorption at  $3100 - 3500 \text{ cm}^{-1}$ . Glc investigation (15% FFAP;  $150^\circ$ ) showed 10% starting material present and 83% of the 1,2-adduct, 1-(1-hexynyl)-3,5,5-trimethylcyclohex-2-en-1-ol. The lack of any absorption in the infrared at  $1710 \text{ cm}^{-1}$  precluded the presence of any 1,4-adduct. A sample of the alcohol collected by preparative glc (15% FFAP;  $120^\circ$ ) was identical to the compound obtained on pg 80.



Reaction of Mesityl Oxide with Diethylhexynylalane.

Diethylhexynylalane (80 mmole) was prepared as outlined previously in a 10:1 ligroin:ether solvent system. The clear supernatant was decanted and then treated with mesityl oxide (3.92 g; 40 mmole) in ligroin (20 ml). After stirring for 4 hr the reaction was worked up as described above. Infrared examination of the crude residue showed no starting enone remaining. Glc investigation (10% QF-1: 105°) showed a 30% yield of the 1,4-adduct 4,4-dimethyldec-5-yn-2-one, and a 40% yield of the 1,2-adduct, 2,4-dimethyldec-5-yn-2-en-4-ol. A sample of the 1,4-adduct was collected by preparative glc (20% FFAP; 105°). ir (liquid film)  $1710\text{ cm}^{-1}$  ( $\text{C}\equiv\text{O}$ ); nmr:  $\tau$  7.52 (s, 2)  $-\text{CH}_2-\text{C}\equiv\text{O}$ , 7.78 (s, 3)  $\text{CH}_3-\text{C}\equiv\text{O}$ , 7.86 (m, 2)  $\text{CH}_2\text{CH}_2-\text{C}\equiv\text{C}$ , 8.62 (m, 4)  $\text{CH}_2\text{CH}_2\text{CH}_2\text{C}\equiv\text{C}$ , 8.75 (s, 6)  $\text{CH}_3-\text{C}-\text{CH}_3$ , 9.1 (t, 3)  $\text{CH}_3-\text{CH}_2$ ; mass spectrum  $m/e$  180(0.2), 165(30), 147(18), 138(25), 133(40), 105(70), 91(55), 81(100), 67(40), 55(45). Anal. Calcd. for  $\text{C}_{12}\text{H}_{20}\text{O}$ : C, 79.94; H, 11.18. Found: C, 80.10; H, 11.07.

A sample of the 1,2-adduct was also collected by preparative glc and proved to be identical with the compound synthesized on pg 81.

Preparation of the 1,2-Adduct of Phenylacetylene with Methyl Isopropenyl Ketone.

A solution of phenylacetylene (4.08 g; 40 mmole) in THF (50 ml) was treated with a solution of *n*-butyllithium in



hexane<sup>21</sup> (40 mmole) at 0°. Methyl isopropenyl ketone (2.94 g; 35 mmole) in THF (20 ml) was slowly added to the resultant solution (0.5 hr). After stirring for 1 hr hydrolysis and examination of an aliquot by infrared spectroscopy showed complete disappearance of carbonyl absorption. The remainder of the reaction mixture was poured into dilute HCl and the two layers were separated. The aqueous phase was extracted with ether (2 x 50 ml) and the combined organic extracts were washed with saturated bicarbonate, water, dried ( $\text{Na}_2\text{SO}_4$ ), and evaporated. Upon distillation, the residue afforded 44 g (67%) 2,3-dimethyl-5-phenylpent-1-en-4-yn-3-ol, bp 118 - 119° (1.5 mm). ir ( $\text{CHCl}_3$ ): 3500 (nonbonded OH), 2230 (C≡C), 1650 (C=C), 1600, 1490, 1450  $\text{cm}^{-1}$  ( $\text{C}_6\text{H}_5$ ); nmr:  $\tau$  2.7 (m, 5)  $\text{C}_6\text{H}_5$ , 4.71 (m, 1)  $\text{HCH}=\text{C}$ , 5.12 (m, 1)  $\text{HCH}=\text{C}$ , 7.12 (s, 1) C-OH, 8.05 (s, 3)  $\text{CH}_3-\text{C}=$ , 8.33 (s, 3),  $\text{CH}_3-\text{C}-\text{OH}$ ; mass spectrum: m/e 186(18), 168(100), 153(35), 152(40), 143(31), 140(30), 128(40), 115(50), 102(60), 85(30), 77(28), 51(25), 43(76). Anal. Calcd. for  $\text{C}_{13}\text{H}_{14}\text{O}$ : C, 83.83; H, 7.58. Found: C, 83.79; H, 7.45.

Reaction Between Methyl Isopropenyl Ketone and Diethylphenylethylnylalane.

Diethylphenylethylnylalane (80 mmole) in a 1:12 ether: ligroin solvent system was prepared as described at the beginning of this experimental section. After being decanted from the precipitated LiCl under  $\text{N}_2$ , the clear supernatant



was cooled to -15°. Methyl isopropenyl ketone (3.36 g; 40 mmole) was added slowly and the solution was stirred for 1.75 hr. Hydrolysis of an aliquot at this time and examination by infrared spectroscopy indicated complete consumption of starting material. The remainder of the reaction mixture was worked up as described above and the yield of 3-methyl-6-phenylhex-5-yn-2-one was estimated as 50% by glc (5% SE30; 150°). A sample was collected by preparative glc and was identical to the compound obtained on pg 75. The amount of 1,2-adduct, 2,3-dimethyl-5-phenylpent-1-en-4-yn-3-ol, was estimated as 38% by glc (5% SE30; 150°). A sample collected by preparative glc was identical to the compound prepared on pg 84.

Preparation of the 1,2-Adduct of Phenylacetylene with Pent-3-en-2-one.

A solution of phenylacetylene (4.08 g; 40 mmole) in THF (50 ml) was treated with a solution of *n*-butyllithium in hexane <sup>21</sup> (40 mmole) at 0°. Pent-3-en-2-one (2.94; 35 mmole) in THF (20 ml) was slowly added to the resultant solution (0.5 hr). After stirring for 1.5 hr the reaction mixture was poured into dilute HCl and the two layers separated. The aqueous phase was extracted with ether (2 x 40 ml) and the combined organic extract was washed with saturated bicarbonate, water, dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated. The residue, upon distillation, afforded 3.9 g (60%) 1-phenyl-2-



methylhex-1-en-4-yn-3-ol, bp 121° (0.5 mm),  $n_D^{25} = 1.5585$ . ir (liquid film) 3200 - 3500 (OH) 2210 (C≡C), 1670 (C=C), 1590, 1490, 1450 cm<sup>-1</sup> (C<sub>6</sub>H<sub>5</sub>); nmr: τ 2.63 (m,5) C<sub>6</sub>H<sub>5</sub>, 3.70 - 4.60 (m,2) CH=CH, 7.41 (s,1) OH, 8.20 (d,3) CH<sub>3</sub>-CH 8.35 (d,3) CH<sub>3</sub>-C-OH; mass spectrum m/e 186(20), 185(30), 168(100), 167(90), 153(55), 152(70), 141(30), 128(50), 115(40), 102(35), 63(25), 51(30), 43(60), 18(55). Anal. Calcd. for C<sub>13</sub>H<sub>14</sub>O: C, 83.83; H, 7.58. Found: C, 83.95; H, 7.78.

#### Reaction of Diethylphenylethylnylalane with Pent-3-en-2-one

Diethylphenylethylnylalane (80 mmole) in a 12:1 ligroin:ether solvent system was prepared as described at the beginning of this experimental section. After decantation under N<sub>2</sub> from the precipitated LiCl the clear supernatant was cooled to -15°. Pent-3-en-2-one (3.36 g; 40 mmole) in ligroin (20 ml) was slowly added to the cooled solution. After stirring for 1 hr the reaction mixture was worked up as described above. Glc examination (5% SE30; 150°) indicated a yield of 54% of the 1,4-adduct, 4-methyl-6-phenylhex-5-yn-2-one. A sample was collected by preparative glc (10% SE30; 200°) and was identical to the sample isolated on pg 76. The 1,2-adduct, 1-phenyl-2-methylhex-1-en-4-yn-ol [11% by glc (5% SE30; 130°)] was collected by preparative glc (5% SE30: 100°) and proved identical to the compound prepared above.



Reaction of Diethylphenylethylnylalane with 1-Acetylcylohexene in a 1:1 Ratio.

Diethylhexynylalane (30 mmole) in a 15:1 ligroin:ether solvent system was made as described above. 1-Acetyl-cyclohexene (3.72 g; 30 mmole) in ligroin (15 ml) was added slowly (0.5 hr) to the above suspension without prior decantation from the precipitated LiCl. After stirring a further 1.75 hr an aliquot was hydrolysed and infrared examination showed complete consumption of starting material. The remainder of the reaction mixture was worked up as described above and the yield of 2-(1-hexynyl)acetylcylohexane was determined as 68% by glc (10% SE30: 200°). A sample collected by preparative glc (10% SE30; 190°) proved identical with the compound obtained on pg 72.

Reaction of Diethylphenylethylynnylalane with Benzalacetophenone in a 1:1 ratio.

Diethylphenylethylnylalane (40 mmole) in a 12:1 ligroin:ether solvent system was prepared as described previously. Without prior decantation, the heterogeneous mixture of LiCl and alane solution was treated with benzalacetophenone (8.32 g; 40 mmole) in benzene (35 ml) over 1 hr. After stirring an additional 0.5 hr hydrolysis of an aliquot and examination by infrared spectroscopy indicated complete consumption of starting enone. The reaction mixture was poured carefully into ice:concentrated HCl and then cooled for 4 hr in the refrigerator. The white crystals were collected by vacuum



filtration and recrystallized from benzene:pentane (1:3 by volume) to give 10.5 g (85%) 1,3,5-triphenylpent-4-yn-1-one, mp 94 - 94.5°, identical in all respects with the compound obtained on pg 75.

Reaction of Diethylphenylethylnylalane with 1-Acetylcylohexene in 3:1 Diethylether:Ligroin Solvent System.

Diethylphenylethylnylalane (18 mmole) in a 3:1 ether:ligroin solvent system was prepared as described at the beginning of this experimental section. After decantation under N<sub>2</sub> from the precipitated LiCl, the clear supernatant was cooled to -15° and 1-acetylcylohexene (1.10 g; 9 mmole) in ether (10 ml) was slowly added. After 1.25 hr the reaction mixture was worked up as described above. The yellow oil so obtained contained 94% of the conjugate adduct, 2-(1-hexynyl)acetylcylohexane, by glc (5% SE30; 220°). Distillation of the crude oil afforded 1.4 g (69%) of the 1,4-adduct, bp 138-140° (140 μ), identical to the sample obtained on pg 72.

Reaction of Methyl Isopropenyl Ketone with Diethylphenylethylnylalane in a 3:1 Diethyl Ether:Ligroin Solvent System.

Diethylphenylethylnylalane (20 mmole) in a 3:1 ether:ligroin solvent system was prepared as described at the outset of this experimental section. After decantation under N<sub>2</sub> from the precipitated LiCl the clear supernatant



was cooled to -15° and methyl isopropenyl ketone (0.84 g; 10 mmole) was dissolved in ether (10 ml) and slowly added. After stirring at this temperature for 1.25 hr the reaction mixture was worked up as described above. The yield of 3-methyl-5-phenylhex-5-yn-2-one in the residue was determined as 23% by glc (5% SE30; 210°). A sample isolated by preparative glc (5% SE30; 205°) was identical with the compound obtained on pg 77.

Reaction of Pent-3-en-2-one with Diethylphenylethylnylalane  
in a 3:1 Diethylether:Ligroin Solvent System.

Diethylphenylethylnylalane (20 mmole) in a 3:1 ether:ligroin solvent system was prepared as described previously. After decantation under N<sub>2</sub> from the precipitated LiCl the clear supernatant was cooled to -15° and pent-3-en-2-one (0.84 g; 10 mmole) in ether (10 ml) was slowly added. After stirring for 1.25 hr the reaction mixture was worked up as described above. The yield of 4-methyl-6-phenylhex-5-yn-2-one in the residue was determined as 37% by glc (5% SE30; 210°). A sample isolated by preparative glc (5% SE30; 205°) was identical with the compound obtained on pg 78.

Reaction of Diethylphenylethylnylalane with Cinnamaldehyde

Diethylphenylethylnylalane (60 mmole) in a 11:1 ligroin:ether solvent system was prepared as described above. After decantation under N<sub>2</sub> from the precipitated LiCl the clear



supernatant was cooled to  $\sim -5^\circ$ . Cinnamaldehyde (3.96 g; 30 mmole) in 1:1 ligroin:ether (40 ml) was added slowly with stirring to the above solution. A brown colouration appeared upon the addition of the enal to the aluminum reagent but rapidly dissipated. After stirring for 1 hr at this temperature an aliquot was withdrawn and hydrolysed. Examination by infrared spectroscopy showed no absorption in the carbonyl region. The remainder of the reaction mixture was worked up as described above. The residue was chromatographed over neutral (Woelm) alumina (Activity III) using benzene : pentane (1:1 by volume) and then ether as eluant. After recrystallization from chloroform:pentane (1:3 by volume) there was obtained 10 g (43% yield) of the 1,2-adduct, 1,5-diphenylpent-1-yn-4-en-2-ol. ir ( $\text{CHCl}_3$ ): 3000 (nonbonded OH), 2220 ( $\text{C}\equiv\text{C}$ ), 1600, 1490, 1450  $\text{cm}^{-1}$  ( $\text{C}_6\text{H}_5$ ); nmr:  $\tau$  2.74 (m,10)  $\text{C}_6\text{H}_5^x$  2, 3.22 (d,1)  $\text{CH}=\text{CH}$ , 3.72 (q,1)  $\text{CH}-\text{CH}=\text{CH}$ , 4.74 (d,1)  $\text{HOCH}-\text{CH}=$ , 7.86 (s,1) C-O ; mass spectrum  $m/e$  234(75), 215(36), 205(45), 191(24), 129(100), 115(40), 102(82), 91(60), 77(58), 51(30). Anal. Calcd. for  $\text{C}_{17}\text{H}_{14}\text{O}$ : C, 87.15; H, 5.82; Found: C, 87.29; H, 5.82.

Reaction of Diethylphenylethylnylalane with 4-Phenyl-3-butyn-2-one.

Diethylphenylethylnylalane (40 mmole) was prepared in a solvent system of 10:1 ligroin:ether as previously described. After decantation under  $\text{N}_2$  from the precipitated LiCl the clear supernatant was cooled to  $0^\circ$ . 4-Phenyl-3-butyn-2-one



(2.88 g; 20 mmole) in ligroin (10 ml) was slowly added. The reaction mixture turned a deep amber colour. After stirring for 0.5 hr at this temperature hydrolysis of an aliquot and examination by infrared spectroscopy showed no carbonyl absorption. The remainder of the amber solution was worked up as described above to afford a yellow, oily residue. This was chromatographed over neutral (Woelm) alumina (Activity III) using pentane:benzene (2:1 by volume) as eluant. The crude 1,5-diphenyl-3-methylpenta-1,4-diyn-3-ol was recrystallized from chloroform:pentane (1:3 by volume) to afford 2.94 g (60%) of white needles, mp 109.5-110.5°. ir ( $\text{CHCl}_3$ ) 3600 (nonbonded OH), 2040 (C C), 1600, 1490, 1440  $\text{cm}^{-1}$  ( $\text{C}_6\text{H}_5$ ); nmr:  $\tau$  2.59 (m,10)  $\text{C}_6^H\text{H}_5 \times 2$ . 7.26 (s,1) OH, 8.05 (s,3)  $\text{CH}_3\text{-C-OH}$ ; mass spectrum:  $m/e$  246(5.3), 231(40), 203(42), 202(40), 144(15), 129(100), 102(61), 75(32), 51(27), 43(30). Anal. Calcd. for  $\text{C}_{18}\text{H}_{14}\text{O}$ : C, 87.78; H, 5.73. Found: C, 88.04; H, 5.63.

Reaction of Diethylphenylethylnylalane with 1-Acetylcyclohexene in the Presence of Galvinoxyl.

To a lithium chloride-free solution of diethylphenylethylnylalane (40 mmole) in a 10:1 ligroin:ether solvent system at -20° was added five mole percent of Galvinoxyl (0.41 g; 1 mmole). This caused the alane solution to take on a deep purple colouration. 1-Acetylcyclohexene (2.48 g; 20 mmole) in ligroin (10 ml) was slowly added at this temperature, and



after stirring 2.5 hr the colour had changed from purple to pale green. Decalin (2.76 g; 20 mmole) was added as an internal standard and an aliquot was hydrolysed and examined by infrared spectroscopy. No starting material carbonyl absorption was apparent, indicating completion of the reaction. A yield of 96% of 2-(phenylethynyl)acetylcyclohexane was determined by glc (10% SE30; 200°). A sample of the 1,4-adduct isolated by preparative glc (10% SE30; 190°) proved identical to a sample of the compound prepared on pg 72.

Reaction of Diethylphenylethynylalane with Pent-3-en-2-one  
in the Presence of Galvinoxyl.

Diethylphenylethynylalane (30 mmole) in a 10:1 ligroin:ether solvent system free of LiCl was prepared as described above and cooled to -15°. Five mole percent galvinoxyl (0.309 g; 0.7 mmole) was added, which caused the clear alane solution to take on a deep purple colouration. Pent-3-en-2-one (1.26 g; 15 mmole) in ligroin (10 ml) was slowly added, and after stirring at this temperature for 1.5 hr an aliquot was hydrolysed. Infrared examination showed lack of starting material absorption. The remainder of the reaction mixture was worked up as described above and made up to 100 ml in a volumetric flask. A yield of 45% of 4-methyl-6-phenylhex-5-yn-2-one was detected by glc (10% QF-1; 170°). A sample of 1,4-adduct isolated by preparative glc (10% QF-1; 140°) was identical with the compound obtained on pg 78.



Reaction Between Diethylhexynylalane and 1-Acetylcyclohexene in the Presence of Styrene.

In order to ascertain that styrene monomer was stable to the alane reagent and the reaction workup conditions the following blank was performed.

Diethylhexynylalane (20 mmole) in a 10:1 ligroin:ether solvent system was prepared as described at the beginning of this experimental section. After decantation under N<sub>2</sub> the clear supernatant was stirred with styrene (2.00 g; 20 mmole) at -20° for 2.5 hr. The reaction mixture was hydrolysed by pouring into ice:concentrated HCl and concentrated *in vacuo* at room temperature to avoid thermal polymerization of the styrene. The quantity of styrene recovered was quantitative as indicated by ultraviolet spectroscopy.

Diethylhexynylalane (30 mmole) in a 10:1 ligroin:ether solvent system was prepared as previously described. After decantation under N<sub>2</sub> and cooling to -15° the clear supernatant was treated with styrene (3.09 g; 30 mmole). 1-Acetylcyclohexene (2.26 g; 18 mmole) in ligroin (15 ml) was added slowly. After stirring for 2 hr the reaction mixture was worked up as described above. Ultraviolet spectroscopic estimation of the amount of styrene present in the crude was 100%. The yield of 2-(1-hexynyl)acetyl-cyclohexane was determined as 79% by glc (5% SE30; 180°). A sample isolated by preparative glc (10% SE30; 190°) was



identical with the compound obtained on pg 69.

Reaction of Diethylphenylethylnylalane with Pent-3-en-2-one  
in the Presence of Styrene.

Diethylphenylethylnylalane (40 mmole) was prepared in 11:1 ligrion:ether solvent system as described above. After decantation under  $N_2$  from the precipitated LiCl, the clear supernatant was cooled to  $-20^\circ$  and styrene (3.6 g; 18 mmole) was added. Pent-3-en-2-one (1.68 g; 20 mmole) in ligroin (10 ml) was slowly added and the mixture was stirred for 2.25 hr. The reaction mixture was then worked up as described above and the amount of styrene recovered was determined as 100% by ultraviolet spectroscopy. The amount of 4-methyl-6-phenylhex-5-yn-2-one present in the crude residue was estimated as 42% by glc (10% QF-1; 170°). A sample isolated by preparative glc (10% QF-1; 175°) was identical to the compound obtained on pg 78.

Reaction of Tri-*n*-butylborane with Methyl Vinyl Ketone in  
the Presence of Styrene.

In order to establish that styrene monomer was stable in the presence of the borane, the following blank was performed.

Tri-*n*-butylborane <sup>21</sup> (15 mmole) in THF (25 ml) was stirred with water (.27 ml; 15 mmole) and styrene (2.81 g; 28 mmole) for 3 hr at 25°. The solution was then made up to 100 ml in a volumetric flask and the amount of styrene



present was determined as 2.8 g by ultraviolet spectroscopy (100% recovery).

Styrene (2.81 g; 28 mmole) and water (.27 ml; 15 mmole) were added to tri-*n*-butylborane<sup>21</sup> (15 mmole) dissolved in THF (25 ml). Methyl vinyl ketone (2.10 g; 30 mmole) in THF (10 ml) was added slowly at 25° and the reaction stirred overnight. The reaction mixture was then made up to 100 ml in a volumetric flask and the quantity of styrene present determined as 1.76 g by ultraviolet spectroscopy. Thus there was 37% polymerization. The yield of 2-octanone was 36% by glc (10% NPGSE; 180°). A sample collected by preparative glc (10% NPGSE; 200°) was identical with authentic 2-octanone.

Attempted Hydration of 1,3,5-Triphenylpent-4-yn-1-one.

1,3,5-Triphenylpent-4-yn-1-one (5 g; 1.6 mmole) was dissolved in 50 ml of 70% aqueous methanol with warming (to aid solution). Then mercuric sulfate (0.08 g) and sulfuric acid (0.05 g) were added and the mixture refluxed for 5 hrs. The reaction mixture was then concentrated *in vacuo* and diluted with water. The resultant suspension was extracted with ether (3 x 30 ml) and the combined extracts washed with saturated bicarbonate, water, dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated. This afforded a brown oil which was induced to crystallize by taking it up in a little ether and adding pentane. After recrystallization from ether:pentane (1:3 by volume) there was obtained 3.85 g



(77%) of a solid mp 93 - 94°, identical with the starting material.

Hydration of 1,3,5-Triphenylpent-4-yn-1-one.

1,3,5-Triphenylpent-4-yn-1-one (5 g; 1.6 mmole) was dissolved in 90% acetic acid (150 ml). Then mercuric acetate (0.75 g) and sulfuric acid (0.05 g) were added. The mixture was refluxed for 6 hr at which point examination of the reaction mixture by tlc (silica gel eluted with 1:1 benzene:Skelly B by volume) showed absence of starting material. The solution was cooled and poured into water (500 ml). The resultant mixture was extracted with ether (6 x 50 ml) and the combined extracts were washed carefully with saturated bicarbonate until neutral. They were then washed with water, dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated to afford a brown oil which exhibited no carbonyl absorption in the infrared.

Hydration of 1,3,5-Triphenylpent-4-yn-1-one.

1,3,5-Triphenylpent-4-yn-1-one (5 g; 1.6 mmole) was dissolved in hot 95% ethanol (275 ml). Then mercuric sulfate (0.6 g) and sulfuric acid (0.5 g) along with water (30 ml) were added and the resultant solution refluxed for 14 hr. The solution was then neutralized with saturated bicarbonate and diluted with water (500 ml). This was extracted with chloroform (4 x 50 ml) and the combined extracts were dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated to



afford 1,3,5-triphenylpenta-1,4-dione as white crystals. Recrystallization from chloroform:pentane (1:3 by volume) gave 5 g (95%) white needles, mp 86.5 - 87°. ir (CHCl<sub>3</sub>) 1720 (C=O) 1680 cm<sup>-1</sup> (Ar C=O); nmr: τ 2.0 - 3.0 (m, 15) C<sub>6</sub>H<sub>5</sub> × 3, 5.51 (q, 1) O=C-CH-CH<sub>2</sub>, 5.95 (q, 1) CH-HCH-C=O, 6.21 (s, 2) C<sub>6</sub>H<sub>5</sub>-CH<sub>2</sub>-C=O, 6.92 (q, 1) CH-HCH-C=O; mass spectrum (Calcd. for C<sub>23</sub>H<sub>20</sub>O<sub>2</sub>: 328.1463; Found: 328.1457): m/e 328(2), 238(13), 237(72), 210(14), 106(21), 105(100), 91(53), 77(75). Anal. Calcd. for C<sub>23</sub>H<sub>20</sub>O<sub>2</sub>: C, 84.12; H, 6.14; Found: C, 83.89; H, 6.19.

#### Attempted Cyclization of 1,3,5-Triphenylpenta-1,4-dione.

1,3,5-Triphenylpenta-1,4-dione (3 g; 0.92 mmole) was dissolved in 75 ml ethanol while warming to aid solution. Ethanolic sodium hydroxide (150 ml of a 2% solution) was slowly added and the resultant solution was stirred at 25° overnight. The reaction was then neutralized with 1N HCl and extracted with chloroform (4 x 50 ml). The combined extracts were dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated to afford a brown oil which exhibited no absorption in the carbonyl region in the infrared spectrum.

#### Cyclization of 1,3,5-Triphenylpenta-1,4-dione.

1,3,5-Triphenylpenta-1,4-dione (990 mg; 0.3 mmole) was dissolved with warming in alcoholic sodium hydroxide (125 ml of a 2% solution). The amber solution was refluxed for 1.5 hr, then cooled, neutralized with 1N HCl



and extracted with chloroform ( $3 \times 25$  ml). The extracts were dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated to afford an oil which could be induced to crystallize by taking it up in a small volume of chloroform and adding pentane. 2,3,5-Triphenylcyclopent-2-en-1-one 560 mg (60%) was isolated. Recrystallization from benzene:pentane (1:3 by volume) gave white prisms mp 153 - 154.5° ir ( $\text{CHCl}_3$ ) 1705 (C=O), 1630 (C=C), 1600, 1580, 1480, 1450  $\text{cm}^{-1}$  ( $\text{C}_6\text{H}_5$ ); nmr:  $\tau$  2.75 (m,15)  $\text{C}_6\text{H}_5 \times 3$ , 6.15 (q,1)  $\text{C}_6\text{H}_5-\text{CH}-\text{HCH}$ , 6.45 (q,1)  $\text{C}_6\text{H}_4\text{CH}-\text{HCH}$ , 6.93 (q,1)  $\text{C}_6\text{H}_5-\text{CH}-\text{HCH}$ ; mass spectrum (Calcd. for  $\text{C}_{23}\text{H}_{18}\text{O}$  310.1358; found: 310.1351)  $m/e$  310(100), 281(12), 203(13), 191(32), 178(34), 105(45), 102(19), 91(18), 77(27). Anal. Calcd. for  $\text{C}_{23}\text{H}_{18}\text{O}$ : C, 89.00; H, 5.85; Found: C, 88.86; H, 5.80.

#### Cyclization of 1,3,5-Triphenylpenta-1,4-dione.

1,3,5-Triphenylpenta-1,4-dione (1.0 g; 0.3 mmole) was dissolved with warming in methanol (30 ml) under  $\text{N}_2$ . Alcoholic sodium hydroxide (10 ml of a 4% solution in methanol) was then added and the yellow solution refluxed for 1 hr. Thin layer examination (silica gel eluted with 1:1 ethyl ether: pentane) indicated complete consumption of starting material. The reaction mixture was acidified with dilute HCl (2N) and the precipitate was extracted with chloroform. The extracts were dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated and the crude residue recrystallized from chloroform:heptane (1:3 by volume) to



afford 790 mg (85%) 2,3,5-triphenylcyclopent-2-en-1-one,  
mp 153-154.5°, identical to the product obtained above.



THE REACTION OF DIALKYLALKENYLALANE REAGENTS WITH  
CONJUGATED ENONES. A METHOD FOR THE 1,4-ADDITION  
OF ALKENE UNITS TO SIMPLE  $\alpha$ , $\beta$ -UNSATURATED KETONES

I N T R O D U C T I O N

The success of dialkylalkynylalanes at selectively achieving the conjugate addition of the alkynyl moiety to  $\alpha$ , $\beta$ -unsaturated ketones suggested the possibility of using other unsaturated organoaluminum species in a like manner. Wilke and coworkers<sup>59-62</sup> have demonstrated that vinylalanes are readily obtainable by the hydroalumination of acetylenes with dialkylaluminum hydrides. As was mentioned in the first part of this Chapter, Zweifel and coworkers<sup>33-35</sup> have demonstrated that these alkenylalanes undergo preferential scission of the vinylcarbon-aluminum bond with such reagents as carbon dioxide, halogen, cyanoxygen and aldehydes and ketones to afford ethylenic acids, halides, nitriles and alcohols, respectively. (In certain cases higher yields are obtained when the preformed aluminate complex is employed). The question thus arose as to whether or not such a vinylalane species might be capable of selectively transferring the vinyl moiety to the  $\beta$ -carbon of an enone system.

Such a reaction, if achieved with retention of the configuration of the vinyl group in the alane, would allow the stereospecific introduction of di- and trisubstituted

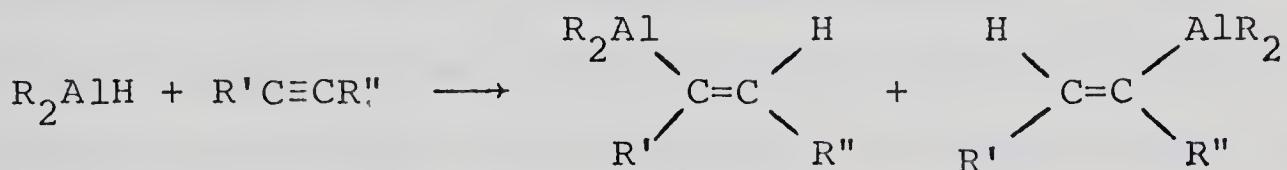


olefin moieties into the enone molecule. It has been mentioned previously that alkenylcuprates apparently add the alkenyl moiety conjugately to an enone system with retention of configuration. Vinyl lithium species are used to generate the cuprate. However, though generation of an isomerically pure alkenyllithium organometallic is possible it requires the prior availability of the isomerically pure alkenyl halide. Use of an alkenylalane offered the possibility of obviating the intermediate steps necessitated by the use of an alkenylcuprate for conjugate addition. Consequently a brief investigation was conducted into the reaction of dialkyl-alkenylalanes with  $\alpha,\beta$ -unsaturated ketones.

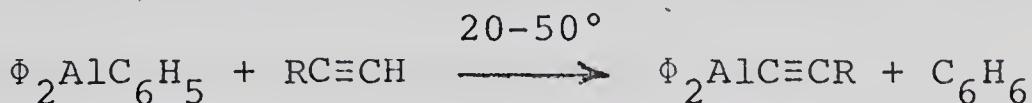


R E S U L T S   A N D   D I S C U S S I O N

To obtain dialkylalkenylalanes, Wilke has reacted terminal and internal acetylenes with both diisobutyl-aluminum hydride and trialkylaluminum reagents. The reactions are done in the absence of any solvent. When they are conducted in the range of 0-50° the exclusive or predominant reaction is a clean 1:1 *cis*-addition of the organoaluminum compound across the triple bond. <sup>59-62</sup>



Other workers have noted that there appear to be exceptions to this reaction. Eisch and Kaska <sup>63</sup> report that triphenylaluminum metalates terminal alkynes, such as 1-hexyne and phenylacetylene, quite readily in benzene solution:



$$R = n-C_4H_9, C_6H_5$$

Zakharkin and coworkers <sup>64</sup> report that the reaction of diethyl- or diisobutylaluminum hydride with alkynes leads to mono- and diaddition of the hydride to the acetylene, as well as metallation. Metallation is predominant



with the more acidic phenylacetylene. Surtees<sup>65</sup> has also surveyed the reaction of phenylacetylene with a variety of dialkylaluminum hydrides and reports varying amounts of metallation.

Because of the reported variability as to the nature of the reaction of a dialkylaluminum hydride with phenylacetylene, it was decided for the purpose of this investigation to utilize the less acidic alkyne 1-hexyne.

In general, the procedure for hydroalumination was patterned after that of Zweifel and coworkers. They employed a hydrocarbon solvent for the hydroalumination. In order to minimize the possibility of complicating side reactions such as metallation and dihydroalumination, temperatures above 55-60° were avoided. We have observed that addition of the diisobutylaluminum hydride to a concentrated (>4 M) solution of the alkyne in hydrocarbon solvent was a very exothermic reaction and led to rapid formation of the dialkylalkenylalane. Dilution of the alkyne solution, however, resulted in incomplete reaction. Heating the reaction mixture at 50-60° prior to its reaction with the enone substrate ensured complete hydroalumination.

Diisobutylhexenylalane was heated with benzalacetone at room temperature. After 1.25 hr of reaction, hydrolysis of an aliquot indicated complete consumption of starting



material. Upon workup (in a manner similar to that employed for the alkynylalane reactions performed previously), glc analysis showed a 67% yield of the conjugate adduct, 4-phenyl-5-decen-2-one. The nmr spectrum showed that the coupling constant of the two vinyl protons was of the order of 15 cps - indicating they were disposed in a *trans* orientation.<sup>66</sup> Thus the *trans* geometry (of the starting vinylalane) had been retained in the product.

With the fact established that a vinylalane transfers the alkenyl moiety with retention of configuration, we then explored this reaction with a variety of enone structural types.

The reaction of diisobutylhexenylalane was carried out with benzalacetophenone. At the end of 1 hr the reaction was complete. An isolated yield of 60% of the conjugate adduct, 1,3-diphenyl-4-nonen-1-one was obtained. Examination of the nmr spectrum showed the coupling constant between the two vinyl protons to be 16 cps, again indicative of a *trans* configuration.

Both the cases described above involve enone systems with an aromatic moiety attached to the  $\beta$ -carbon atom. In the case of the dialkylalkynylalane enone reaction, it was this type of compound that gave the highest yield of the conjugate adduct (of the order 65 - 95%). The next type of substrate investigated was an enone system



without any aromatic  $\beta$ -substitution.

1-Acetylhexene was reacted with diisobutylhexenyl-alane. The reaction was complete after 2 hr and glc analysis indicated a yield of 34% of 2-(1-hexenyl)acetyl-cyclohexane.

The reaction was next attempted with methyl vinyl ketone. Reaction with diisobutylhexenylalane under conditions similar to those employed above led to 15% of the conjugate adduct, 5-decen-2-one.

The yields of alkenyl conjugate adduct in the cases of enone substrates without an aromatic substituent in the  $\beta$ -position were thus about 40% lower than their corresponding alkynyl conjugate adducts. By analogy with the alkynylalane reaction, it seemed that the remainder of the unaccounted starting enone was probably being consumed by 1,2-addition (or possibly some form of condensation or polymerization process). Attempts at isolation and characterization of the 1,2-adducts by preparative glc, preparative tlc, column chromatography, or preparation of derivatives (such as trimethylsilyl ethers) all failed. The main problem seemed to be the dehydration of the doubly allylic alcohol to a triene and subsequent polymerization of the triene. As a result, it was not possible to quantitatively assess the amount of 1,2-adduct formed.

In an attempt to minimize the amount of polymerization



or condensation of the starting material the reaction between diisobutylhexenylalane and methyl vinyl ketone was repeated using a much slower addition rate of the enone. However, only a minor improvement (25% yield of 5-decyn-2-one) was achieved over the experiment in which a shorter addition time was employed.

It was then of interest to investigate whether the reactivity of the alkenylalane could be attenuated, and hopefully improve its selectivity for 1,4- over 1,2-addition. Consequently the reaction of the hexenyl-alane with methyl vinyl ketone was repeated, first at lower temperature (-20°), and secondly, in the presence of a Lewis base (diethyl ether). The yields of 5-decyn-2-one were 20 and 29% respectively. In both cases slow addition of methyl vinyl ketone to the alane reagent was employed.

When a stronger Lewis base (i.e. tetrahydrofuran) was employed, the formation of 1,4-adduct was suppressed completely. 1-Acetylhexene was reacted with diisobutylhexenylalane at 25°, and at -25°. In both experiments, the course of reaction was monitored by infrared spectroscopy. In each case there was observed the gradual decrease of carbonyl absorption of starting material, and the gradual increase of hydroxyl absorption. No 1,4-adduct could be detected by glc analysis.

Thus, attempts at increasing the yields of conjugate



adduct by varying temperature, rate of addition or solvent have not met with success.

An interesting facet of the hydroalumination reaction was discovered in an attempt to prepare the vinylalane in ether in the absence of any hydrocarbon solvent.

1-Hexyne was treated with diisobutylaluminum hydride (reflux for 4 hr and stirred for 12 hr at 25°) in ether, and then benzalacetone was added. The product, however, was 4-phenyl-3-buten-2-ol - the simple reduction product of benzalacetone (in 75% yield). Thus the presence of ether appears to greatly diminish the rate of hydroalumination of an alkyne by diisobutylaluminum hydride.

Masamune and coworkers<sup>67</sup> have reported that diisobutylaluminum hydride can be employed to cleanly reduce  $\alpha,\beta$ -unsaturated carbonyl systems to give good yields of the corresponding allylic alcohols. The reaction of the alkenylalane with two representative cyclic enones was then attempted.

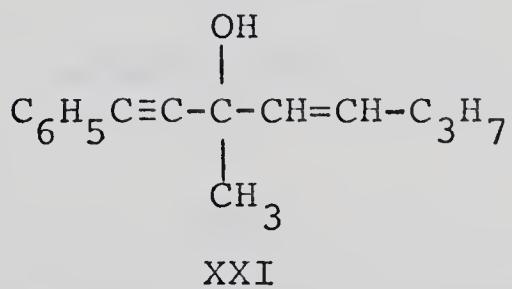
Reaction of 2-cyclohexenone and isophorone, respectively, with diisobutylhexenylalane each gave rise to complex mixtures (four components of *ca.* the same peak area by glc analysis). Although the infrared spectrum of each crude reaction mixture exhibited hydroxyl absorption (3100-3500  $\text{cm}^{-1}$ ), attempts at isolating the (presumed) 1,2-addition products proved fruitless. Despite the con-



ceptual similarity, it is clear, then that the alkenyl-alane-enone system is considerably more complex than the corresponding alkynylalane-enone reaction. In the latter, good yields of 1,2-adducts were obtained (cf. p 65).

Finally a brief investigation of the reaction of a vinylalane with 4-phenyl-3-butyn-2-one and cinnamaldehyde was made. Each was reacted with the alkenylalane formed by the hydroalumination of 1-pentyne with diisobutylaluminum hydride.

The former gave two products, 4-phenyl-3-butyn-2-ol (35%), the product of simple reduction, and the 1,2-adduct (26% yield), 1-phenyl-3-methyloct-1-yn-4-en-3-ol (XXI).

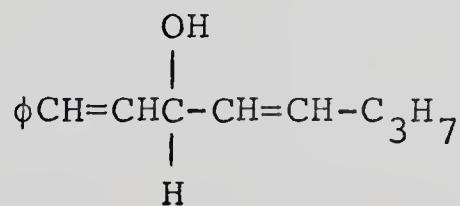


The fact that no 1,4-adduct was observed is consistent with the observation made in the alkynylalane reaction. However, the presence of the reduced ynone in the product mixture can only be rationalized by the presence of excess diisobutylaluminum hydride. Although the hydroalumination reaction was carried out in a manner analogous to previous experiments, 1-pentyne is a much more volatile alkyne.



It is probable that evaporative losses (during reflux) occurred, and the carbinol derives from reaction with diisobutylaluminum hydride.

The reaction of cinnamaldehyde with the pentenyl-alane reagent led to similar results. Upon distillation, two main products were isolated. The lower boiling product proved to be cinnamyl alcohol (40%). Only a very small amount of a higher boiling fraction contaminated with cinnamyl alcohol could be isolated. Attempts to eliminate the small amounts of cinnamyl alcohol impurity proved unsuccessful. However, on the basis of nmr spectroscopy the product is tentatively assigned as 1-phenylocta-1,4-dien-3-ol (XXII).



XXII

It appears from this brief investigation that there are some similarities, as well as important differences, between the reactions of alkenylalane and alkynylalane reagents towards conjugated ketones. Although both reagents give 1,4-adducts toward similar enones the latter system is clearly more efficient. Both systems are highly sensitive toward the nature of solvent (i.e., 1,4-addition is usually suppressed by tetrahydrofuran). The



alkenylalane-enone system gives complex product mixtures in several cases, and products are extremely difficult to isolate. However, in view of the directness with which this method affords *trans*-olefinic ketones in high isomeric purity, it should be of value to the synthetic organic chemist.



EXPERIMENTALGeneral Considerations

Infrared (ir) spectra were recorded using a Perkin-Elmer 337G, Perkin-Elmer 421G or Unicam SP 1000 Infrared Spectrophotometer.

Nuclear magnetic resonance (nmr) spectra were recorded on a Varian A-60 or HR-100 spectrometer. Unless otherwise stated deuteriochloroform ( $\text{CDCl}_3$ ) was employed as the solvent with tetramethylsilane (TMS) as the internal reference. Chemical shifts are reported as  $\tau$  values relative to TMS = 10. The following abbreviations are used in the text: s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet.

Mass spectra were recorded on an AEI Model MS-2 or Model MS-9 Spectrometer. Spectra are recorded in the following fashion: m/e: peak mass (relative intensity).

Gas liquid chromatography (glc) was performed using an Aerograph A90-P3 and a Varian Aerograph Series 1200 chromatograph.

Refractive indices were measured on a Bausch and Lomb Abbé-3L Refractometer.

Typical Preparation of a Diisobutylalkenylalane.

All operations were carried out under an atmosphere of nitrogen. Diisobutylaluminum hydride <sup>68</sup> (10.7 ml; 60 mmole) was reacted with the appropriate alkyne (70



mmole) for 2 hr at 50° in dry, olefin-free ligroin, according to the method of Zweifel and coworkers. The resulting solution was cooled to 25° and was then ready for reaction with the appropriate substrate.

Typical Workup Procedure for the Reaction Between Diisobutylalkenylalane and  $\alpha$   $\beta$ -Unsaturated Carbonyl Species.

The reaction mixture was carefully poured into ice: concentrated HCl (exothermic). After stirring for 15 minutes the two layers were separated. The aqueous phase was extracted with ether (3 x 30 ml) and the combined organic phase was washed with saturated bicarbonate solution, dried ( $\text{Na}_2\text{SO}_4$ ), and evaporated.

Reaction of Diisobutylhexenylalane with Benzalacetone.

1-Hexyne (9.9 ml; 90 mmole) was reacted with diisobutylaluminum hydride (14.3 ml; 80 mmole) for 2 hr at 50° as described above. A solution of benzalacetone (5.84 g; 40 mmole) in 1:1 ligroin:benzene (20 ml) was slowly added to the resultant solution (0.5 hr) at 25°. A brown colouration which rapidly dissipated was noted upon the addition of each drop of enone to the alane solution. After stirring a further 0.75 hr, hydrolysis of an aliquot and examination by infrared spectroscopy indicated complete consumption of the starting material. The mixture was worked up as described above. Analysis



of the residue by glc (10% QF-1; 100°) showed a 67% yield of the conjugate adduct, 4-phenyl-5-decen-2-one. A sample was collected by preparative glc (5% SE30; 220°). ir (thin film) 1710 (C=O), 1600, 1490, 1450, 970, 700 cm<sup>-1</sup> (C<sub>6</sub>H<sub>5</sub>); nmr τ: 2.85 (s,5) C<sub>6</sub>H<sub>5</sub>, 4.55 (m,2) -CH=CH-, 6.21 (q,1) C=CH-CH-C<sub>6</sub>H<sub>5</sub>, 7.25 (d,2) O=C-CH<sub>2</sub>CH, 8.02 (s,3) CH<sub>3</sub>C=O, 8.05 (m,2) -CH<sub>2</sub>-CH=, 8.75 (m,4) CH<sub>2</sub>CH<sub>2</sub>, 9.2 (t,3) CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>; mass spectrum m/e: 230(25), 215(8), 187(12), 172(38), 159(31), 143(14), 131(34), 129(35), 117(71), 105(16), 91(71), 43(100). Anal. Calcd. for C<sub>16</sub>H<sub>22</sub>O: C, 83.43; M, 9.63: Found: C, 83.79; H, 9.50.

Reaction of Diisobutylhexenylalane with Benzalacetophenone.

1-Hexyne (5.5 ml; 50 mmole) was reacted with diisobutylaluminum hydride (7.15 ml; 40 mmole) in ligroin (30 ml) for 2 hr at 50° as described above. A solution of benzalacetophenone (4.16 g; 20 mmole) in 2:1 benzene: ligroin (15 ml) was added slowly to the resultant solution at 25°. At the end of 1 hr hydrolysis of an aliquot and examination by infrared spectroscopy indicated complete consumption of starting material. The reaction was worked up as described above to afford 6.30 g crude product. A small portion (975 mg) was subjected to preparative thin layer (silica gel elution with benzene



followed by 1:1 benzene:ligroin by volume) and afforded 532 mg (60%) of the conjugate adduct, 1,3-diphenyl-4-nonen-1-one. ir (thin film) 1685 (aromatic C=O), 1600, 1490, 1450, 750  $\text{cm}^{-1}$  ( $\text{C}_6\text{H}_5$ ); nmr  $\tau$ : 2.0 - 2.85 (m,10)  $\text{C}_6\text{H}_5 \times 2$ , 6.45 (m,2)  $-\text{CH}=\text{CH}-$ , 5.90 (q,1)  $\text{CH}-\text{CH}_2$ , 6.65 (d,2)  $\text{CH}_2-\text{CH}-\text{C}_6\text{H}_5$ , 8.0 (m,2)  $-\text{CH}_2-\text{CH}=\text{CH}$ , 8.71 (m,4)  $-\text{CH}_2\text{CH}_2-$ , 9.11 (t,3)  $\text{CH}_3\text{CH}_2-$ ; mass spectrum  $m/e$ : 292(10), 221(9), 167(6), 105(100), 91(11), 77(18), 58(15).

Reaction of Diisobutylhexenylalane with 1-Acetylcylohexene.

1-Hexyne (7.7 ml; 70 mmole) was reacted with diisobutylaluminum hydride (10.5 ml; 60 mmole) in ligroin (30 ml) at 50° for 2 hr as described above. A solution of 1-acetylcylohexene (3.72 g; 30 mmole) in 1:1 ligroin:benzene (10 ml) was slowly added (0.25 hr) to the resultant solution at 20°. After 2 hr hydrolysis of an aliquot and examination by infrared spectroscopy showed complete disappearance of starting material carbonyl peak. The reaction mixture was worked up as described above and the yield of the conjugate adduct, 2-(1-hexenyl)acetylcylohexane was estimated as 34% by glc (10% SE30; 190°). A sample was collected by preparative glc (20% SE30; 200°). ir (thin film) 1710  $\text{cm}^{-1}$  (C=O); nmr  $\tau$ : 4.70 (m,2)  $\text{CH}=\text{CH}-$ , 7.99 (s,3)  $\text{CH}_3-\text{C=O}$ , 7.70 - 8.90 (m,16)  $\text{CH}_3-$ , 9.10 (t,3)  $\text{CH}_3-\text{CH}_2$ ; mass



spectrum  $m/e$ : 206(27), 191(8), 188(7), 164(45), 150(19), 146(12), 137(15), 123(16), 109(36), 95(50), 83(22), 81(10), 79(21), 67(42), 55(38), 43(100). Anal. Calcd. for  $C_{14}H_{24}O$ : C, 80.71; H, 11.61. Found: C, 80.46; H, 11.67.

Reaction of Diisobutylhexenylalane with Methyl Vinyl Ketone.

1-Hexyne (9.9 ml; 90 mmole) was reacted with diisobutylaluminum hydride (14 ml; 80 mmole) in ligroin (40 ml) at 50° for 2 hr. A solution of methyl vinyl ketone (2.80 g; 40 mmole) in 1:1 benzene:ligroin (15 ml) was slowly added (0.5 hr) at 25°. After 2.5 hr the reaction was worked up and the yield of 5-decen-2-one in the residue was determined as 15% by glc (10% SE30; 105°). A sample was isolated by preparative glc (20% SE30; 165°). ir (thin film)  $1715\text{ cm}^{-1}$  ( $\text{C=O}$ ); nmr  $\tau$ : 4.55 (m,2)  $\text{CH=CH}$ , 7.40 - 8.20 (m,6)  $\text{CH}_2-\text{CH}_2-\text{CH=CH-CH}_2$ , 7.85 (s,3)  $\text{CH}_3\text{C=O}$ , 8.66 (m,4)  $\text{CH}_2\text{CH}_2$ , 9.10 (t,3)  $\text{CH}_3\text{CH}_2$ ; mass spectrum  $m/e$ : 154(12), 111(12), 97(26), 96(52), 81(35), 71(17), 69(20), 67(25), 54(50), 43(100), 41(31). Anal. Calcd. for  $C_{10}H_{18}O$ : C, 77.87; H, 11.76. Found: C, 77.83; H, 11.68.

Reaction of Diisobutylhexenylalane with Methyl Vinyl Ketone.

1-Hexyne (6.05 ml; 55 mmole) was reacted with diisobutylaluminum hydride (8.7 ml; 50 mmole) in ligroin (40



ml) at 50° for 2 hr. A solution of methyl vinyl ketone (1.75 g; 25 mmole) in 1:1 benzene:ligroin (50 ml) was added slowly over a period of 3 hr at 25°. The resultant solution was stirred for 10 hr and then worked up as described above. The yield of 5-decen-2-one in the residue was determined as 25% by glc (10% SE30: 105°). A sample was isolated by preparative glc (20% SE30; 165°) and had identical nmr and ir spectra to the compound isolated above.

Reaction of Diisobutylhexenylalane with Methyl Vinyl Ketone at -20°.

1-Hexyne (6.05 ml; 50 mmole) was reacted with diisobutylaluminum hydride (8.7 ml; 50 mmole) in ligroin (40 ml) at 50° for 2 hr. The solution was cooled to -20° and a solution of methyl vinyl ketone (1.75; 25 mmole) in 1:1 benzene:ligroin (50 ml) was slowly added (3 hr) and the resultant solution was stirred for a further 10 hr. After workup the yield of 5-decen-2-one in the residue was determined as 20% by glc (10% SE30; 105°). A sample was isolated by preparative glc (20% SE30; 165°) and had identical nmr and ir spectra to the compound isolated above.

Reaction of Diisobutylhexenylalane with Methyl Vinyl Ketone in Ether.

1-Hexyne (6.05 ml; 55 mmole) was reacted with diiso-



butylaluminum hydride (8.7 ml; 50 mmole) in 1:1 ligroin: benzene (50 ml) at 50° for 2 hr. Ether (50 ml) was added and then a solution of methyl vinyl ketone (1.75 g; 25 mmole) was slowly added over 3 hr. The resulting solution was stirred for 10 hr and then worked up as described above. The yield of 5-decen-2-one in the residue was determined as 29% by glc (10% SE30; 105°). A sample was isolated by preparative glc (20% SE30; 165°) and had identical nmr and ir spectra to the compound isolated above.

Reaction of Diisobutylhexenylalane with 1-Acetylcylohexene.

1-Hexyne (6.05 ml; 55 mmole) was reacted with diisobutylaluminum hydride (8.7 ml; 50 mmole) in 1:1 ligroin: benzene (40 ml) for 2 hr at 50°. The resultant solution was cooled to 20° and a solution of 1-acetylcylohexene (3.1 g; 25 mmole) in ligroin (30 ml) was slowly added over 3 hr. The reaction was stirred for 5 hr and worked up; the yield of 2-(1-hexenyl)acetylcylohexane was 30% by glc (10% SE30; 190°). A sample was isolated by preparative glc (20% SE30; 200°) and had identical nmr and ir spectra to the compound obtained on pg 114.



Attempted Preparation of Diisobutylhexenylalane in Ether  
and Reaction of the Resultant Solution with Benzalacetone.

To a solution of 1-hexyne (7.7 ml; 70 mmole) in ether (50 ml) was slowly added diisobutylaluminum hydride (10.7 ml; 60 mmole). The resultant solution was refluxed ( $36^{\circ}$ ) for 4 hr and then stirred a further 12 hr at  $25^{\circ}$ . Benzalacetone (4.38 g; 30 mmole) in ether (40 ml) was slowly added (1.5 hr) at  $15^{\circ}$ . The resultant solution was stirred for 1 hr and then worked up as described above. Only a trace of the conjugate adduct, 4-phenyl-5-decen-2-one, could be detected by glc (10% QF-1;  $180^{\circ}$ ). The yield of 4-phenyl-3-buten-2-ol was 75% by glc (10% QF-1;  $182^{\circ}$ ). Distillation through a 2 cm vigreux column afforded 4.3 g (60%) of a fraction boiling at  $110-115^{\circ}$  (2 mm) [lit <sup>118</sup> bp  $111-112^{\circ}$  (3 min)]. ir (thin film) 3150-3600 (OH), 1490, 1450, 750,  $690\text{ cm}^{-1}$  ( $C_6H_5$ ); nmr  $\tau$ : 2.69 (s,5)  $C_6H_5^-$ , 3.3 - 4.0 (m,2)  $CH=CH$ , 5.55 (m,1)  $CH_3-CH-CH=C$ , 7.53 (s,1) C-OH, 8.67 (d,3)  $CH_3-CH$ ; mass spectrum  $m/e$ : 148(57), 130(61), 129(75), 115(60), 104(100), 91(62), 87(46), 55(37), 43(98).

Reaction of 2-Cyclohexenone with Diisobutylhexenylalane.

1-Hexyne (4.4 ml; 40 mmole) was reacted with diisobutylaluminum hydride (5.2 ml; 30 mmole) in ligroin (30 ml) at  $50^{\circ}$  for 2 hr. A solution of 2-cyclohexenone (1.45 g; 15 mmole) in 3:1 ligroin:ether (15 ml) was slowly



added at -20° over 1 hr. After stirring for 1 hr, hydrolysis of an aliquot and examination by infrared spectroscopy showed complete lack of carbonyl absorption. The remainder of the reaction mixture was worked up as described above. Attempts at isolation of any of the 4 components seen on the glc trace (10% SE52; 140°) by preparative glc (10% SE52; 150°) and preparative thin layer only led to mixtures containing at least two components.

Reaction of Diisobutylhexenylalane with Isophorone.

1-Hexyne (4.4 ml; 40 mmole) and diisobutylaluminum hydride (5.2 ml; 30 mmole) were reacted in ligroin (30 ml) at 50° for 2 hr. The resultant solution was cooled to -20° and a solution of isophorone (2.10 g; 15 mmole) in 3:1 ligroin:ether (15 ml) was slowly added. The reaction was stirred at this temperature for 3 hr whereupon hydrolysis of an aliquot and examination by infrared spectroscopy showed presence of starting material but no evidence of 1,4 adduct. The reaction was warmed to room temperature and stirred for 21 hr. Workup of the reaction as outlined above afforded a residue which exhibited in the infrared a small amount of starting material carbonyl absorption ( $1680\text{ cm}^{-1}$ ), a large amount of hydroxyl absorption ( $3100 - 3500\text{ cm}^{-1}$ ) but no absorption at  $1710\text{ cm}^{-1}$ . Attempts at isolation and



characterization of any of the five components seen on glc (10% SE52; 160°) by preparative glc (10% SE52; 170°) and preparative thin layer only led to mixtures of at least two components.

Reaction of Diisobutylpentenylalane with 4-Phenyl-3-butyn-2-one.

1-Pentyne (3.30 g; 50 mmole) was reacted with diisobutylaluminum hydride (6.95 ml; 40 mmole) in ligroin (60 ml) at 50° for 2 hr. The resultant solution was cooled to -20° and a solution of 4-phenyl-3-butyn-2-one (2.88 g; 20 mmole) dissolved in ligroin (10 ml) was added slowly (0.75 hr). After 2 hr hydrolysis of an aliquot and examination by infrared spectroscopy showed complete lack of carbonyl absorption. The reaction was worked up as described above and the residue so obtained was subjected to distillation *in vacuo*. The lower boiling fraction bp 59-89° (1 mm) [lit<sup>69</sup> bp 89 (0.75 mm)], isolated in 35% yield, was 4-phenyl-3-butyn-2-ol. ir (thin film) 3100-3500 (OH), 2220 (C≡C), 1600, 1490, 1450, 750, 690 cm<sup>-1</sup> (C<sub>6</sub>H<sub>5</sub>); nmr τ: 2.68 (m, 5) C<sub>6</sub>H<sub>5</sub>-, 5.26 (q, 1) CH-CH<sub>3</sub>, 7.85 (s, 1) CH<sub>3</sub>C-OH, 8.45 (d, 3) CH<sub>3</sub>-CH-OH.

The higher boiling fraction, bp 180-184° (2 mm) isolated in 26% yield, was identified as 3-methyl-1-phenyloct-1-yn-4-en-3-ol. ir (thin film) 3100-3500 (OH), 2220 (C≡C), 1600, 1490, 750, 690 cm<sup>-1</sup> (C<sub>6</sub>H<sub>5</sub>); nmr



$\tau$ : 2.68 (m,5)  $C_6H_5-$ , 3.65 - 4.60 (m,2)  $-CH=C-$ , 7.71 (s,1)  $C=O$ , 8.00 (m,2)  $-CH_2-CH=C$ , 8.35 (s,3)  $CH_3-C-OH$ , 8.60 (m,2)  $CH_3CH_2CH_2$ , 9.10 (t,3)  $CH_3-CH_2-$ ; mass spectrum  $m/e$ : 214(4.1), 196(52), 181(23), 171(59), 164(51), 121(100), 128(53), 103(75), 77(78), 51(55). Anal. Calcd. for  $C_{15}H_{18}O$ : C, 84.07; H, 8.47. Found: C, 83.81; H, 8.20.

#### Reaction of Diisobutylpentenylalane with Cinnamaldehyde

1-Pentyne (3.30 g; 50 mmole) was reacted with diisobutylaluminum hydride (6.95 ml; 40 mmole) in ligroin (60 ml) at 50° for 2 hr. The resultant solution was cooled to -20° and a solution of cinnamaldehyde (2.64 g; 20 mmole) in 1:1 ligroin:ether (20 ml) was added slowly (0.75 hr) at -20°. After stirring for 1.25 hr, hydrolysis of an aliquot and examination by infrared spectroscopy showed disappearance of all carbonyl absorption. The reaction mixture was worked up as described above. Distillation of the residue afforded 1.07 g (40%) cinnamyl alcohol bp 132° (2 mm) [lit <sup>117</sup> bp 257.5 (760)] ir (thin film) 3100-3500 (OH), 1590, 1450, 750, 690  $cm^{-1}$  ( $C_6H_5$ ) nmr  $\tau$ : 2.68 (s,5)  $C_6H_5$ , 3.2 - 4.0 (m,2)  $CH=C$ , 5.71 (d,2)  $C=CH-CH_2$  7.30 (s,1) OH; a higher boiling fraction 0.40 g (18%) contaminated with cinnamyl alcohol, was also isolated (bp 154-160°, 2 mm). By comparison with the nmr of cinnamyl alcohol, this was assigned the



structure of 1-phenylocta-1,4-dien-3-ol from the following nmr data. nmr  $\tau$ : 2.70 (m, 5)  $C_6H_5$ , 3.00 - 4.40 (m, 4)  $CH=CHx2$ , 7.90 (m, 2),  $CH_2CH=C$ , 8.40 (m, 2)  $CH_2CH_2CH_3$ , 9.00 (t, 3)  $CH_3CH_2CH_2$ , 4.32 (m, 1)  $CH-OH$ .

Reaction of Diisobutylhexenylalane with 1-Acetylcyclohexene at -25° in THF.

1-Hexyne (5.5 ml; 50 mmole) was reacted with diisobutylaluminum hydride (6.95 ml; 40 mmole) in ligroin (20 ml for 2 hr at 50°. THF (60 ml) was then added and the resultant solution was cooled to -25°. A solution of 1-acetylcyclohexene (7.48 g; 20 mmole) in THF (15 ml) was slowly added. Hydrolysis of an aliquot and examination by infrared spectroscopy after 1 hr showed some starting material carbonyl at  $1680\text{ cm}^{-1}$ , no carbonyl absorption at  $1710\text{ cm}^{-1}$  but a large amount of hydroxyl absorption at 3100-3000  $\text{cm}^{-1}$ . After 2 hr hydrolysis of an aliquot and examination by infrared showed no carbonyl absorption remaining. The reaction mixture was worked up as described above but attempts at isolation of the 1,2-adduct by distillation and preparative glc only led to polymeric material, presumably from the dehydration and subsequent decomposition of the alcohol.

Reaction of Diisobutylhexenylalane with 1-Acetylcyclohexene at 25° in THF.

1-Hexyne (5.5 ml, 50 mmole) was reacted with diiso-



butylaluminum hydride (6.95 ml; 40 mmole) in ligroin (15 ml) at 50° for 2 hrs. THF (60 ml) was added and then a solution of 1-acetylcyclohexene (2.48 g; 20 mmole) in THF (15 ml) was slowly added (0.75 hr). After stirring for 2 hr, hydrolysis of an aliquot and examination by infrared spectroscopy showed complete disappearance of starting material and appearance of absorption at 1710  $\text{cm}^{-1}$  and 3100 - 3500  $\text{cm}^{-1}$ . The reaction mixture was worked up as described above and glc examination (10% SE30; 190°) of the residue showed no trace of the conjugate adduct, 2-(1-hexenyl)acetylcyclohexane.



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THE UTILITY OF ALKYNYLBORANES IN ORGANIC SYNTHESIS. A

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NOVEL PREPARATION OF PROPARGYLIC ESTERS

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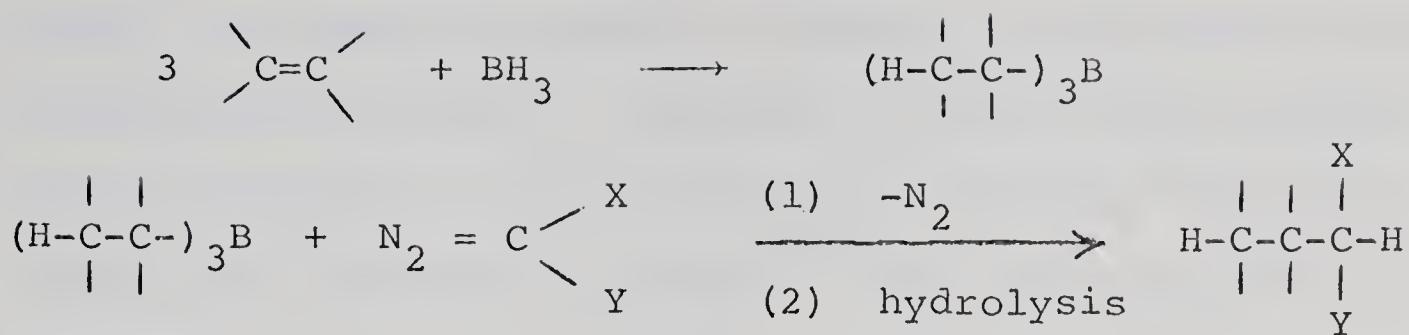
INTRODUCTION

Organoboranes, readily available by the *cis,anti*-Markovnikov addition of borane ( $\text{BH}_3$ ) to olefins<sup>70</sup>, have in recent years proved to be valuable intermediates to the synthetic organic chemist. H. C. Brown and coworkers have conducted studies of a wide range of transformations which can be accomplished using organoboranes. These include:

isomerization<sup>70</sup>; displacement<sup>70</sup>; contrathermodynamic isomerization of olefins<sup>70</sup>; cyclization<sup>71,71</sup>; protonolysis<sup>70</sup>; oxidation to alcohols<sup>70</sup>; oxidation to ketones<sup>70</sup>; amination<sup>73</sup>; metallation<sup>74</sup>; coupling<sup>75,76</sup>; 1,4-addition to  $\alpha,\beta$ -unsaturated aldehydes<sup>47,48</sup>, ketones<sup>46</sup>, and Mannich bases<sup>77</sup>; reaction with ylides<sup>78</sup> or with  $\alpha$ -halo carbanions<sup>79</sup>; and carbonylation<sup>80</sup> to tertiary alcohols, secondary alcohols, ketones, primary alcohols, aldehydes, ring ketones and polycyclics.

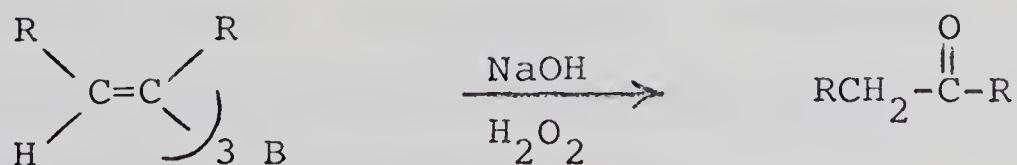
Trialkylboranes have been shown by workers in these laboratories<sup>81,82,83</sup> to react with diazo compounds, affording a convenient and simple method of converting an olefin into a functionalized homolog.





where  $X = H$  and  $Y = CH_3-\overset{\underset{\text{O}}{\parallel}}{C}-$ ,  $C_6H_5\overset{\underset{\text{O}}{\parallel}}{C}-$ ,  $-C\equiv N$ ,  $-COOC_2H_5$ ,  $-\overset{\underset{\text{O}}{\parallel}}{C}- (CH_2)_n-\overset{\underset{\text{O}}{\parallel}}{C}-CHN_2$ , and  $-CHO$ .

Organoboron compounds which possess unsaturated groups bonded to the boron atom have, however, not been as extensively investigated as their saturated counterparts. Brown and Zweifel <sup>84</sup> have reported that the hydroboration of disubstituted acetylenes gives rise to trialkenylboranes as intermediates, which, upon oxidation lead to ketones.



Terminal acetylenes, however, under similar conditions undergo dihydroboration. <sup>85</sup> (Brown and Zweifel report that



use of a hindered organoborane, disiamylborane<sup>86</sup>, will effect a monohydroboration of terminal acetylenes to afford dialkylalkenylboranes. Oxidation of these mixed boranes gives aldehydes in good yields<sup>87</sup>). Gipstein<sup>88</sup> and co-workers and Stafford and Stone<sup>89</sup> have also prepared vinylboranes.

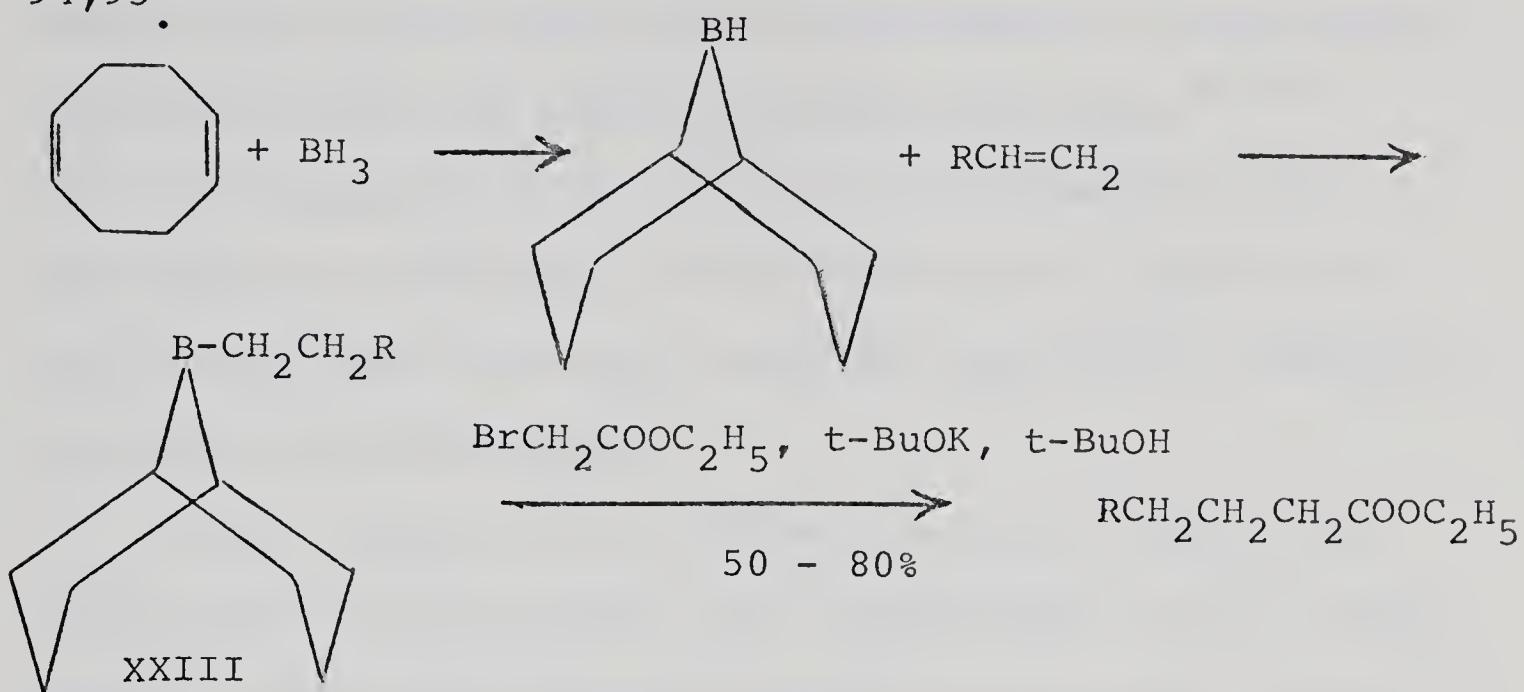
Unsaturated organoboron compounds containing acetylenic moieties attached directly to the boron atom have been prepared by several groups of workers. Soulie and coworkers<sup>90,91</sup> have prepared the pyridine complexes of diphenylakynylboranes,  $(C_6H_5)_2BC\equiv CR \cdot$ pyridine. Hartman and Birr<sup>92</sup> have prepared monoacetylenic boranes of the type  $R_2B-C\equiv CR$ , while Ashby and Foster<sup>93</sup> prepared trialkynylboranes stabilized as amine complexes.

In view of the availability of alkynylboranes it was of interest to investigate their reactions with a diazo substrate such as ethyl diazoacetate in the hope of achieving reaction of an alkynyl moiety to form a homologated alkynyl species (for example, a propargylic ester). To this end a series of trialkynylboranes was prepared and reacted with ethyl diazoacetate. In addition the reaction of a mixed organoborane of the type  $R_2BC\equiv CR'$  with ethyl diazoacetate was attempted.

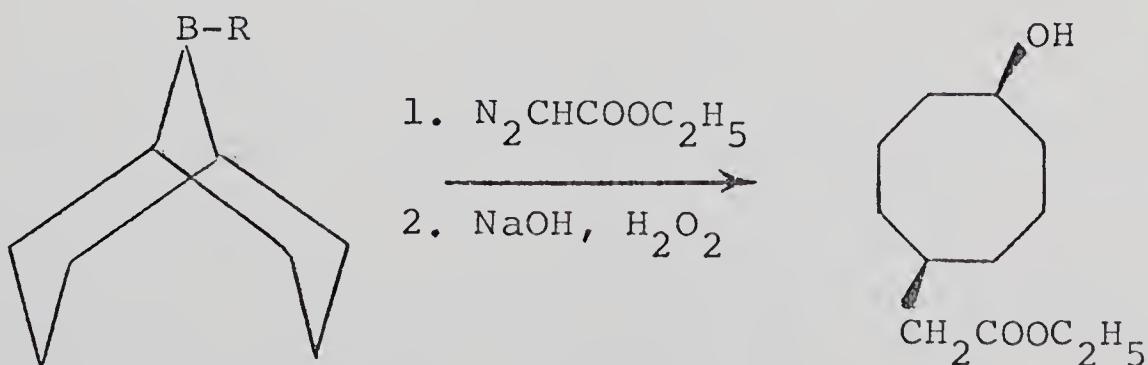
One of the limitations of the reaction of a trialkylborane with a diazo compound and many other substrates is utilization of only one of the three alkyl groups. Conse-



quently the maximum yield obtainable, based on olefin, is necessarily limited to 33.3%. Brown and coworkers have circumvented this problem to a great degree by the use of B-alkyl-9-borabicyclo[3.3.1]nonane (B-alkyl-9-BBN) (XXIII) 94,95.



However, both Brown and Rogić<sup>95</sup> and Hooz and Gunn<sup>96</sup> have reported that the reaction of diazo substrates with B-alkyl-9-BBN derivatives results in the migration of the boron-cyclooctyl bond to afford substituted cyclooctanes.





Morrison<sup>97</sup> attempted to overcome this problem by using a boronic acid diester in the reaction with a diazo substrate. He observed no appreciable reaction and attributed the lack of reactivity of this boron species to a stabilizing effect due to the back-bonding of the oxygen lone pairs into the vacant p-orbital on boron.<sup>98,99</sup> This coordination would decrease the nucleophilicity of the borane to the extent that little or no complexation could occur with the diazo compound and thus no subsequent reaction could take place.

It was thought that another electron-withdrawing group (other than alkoxy) as a substituent on the borane might increase its electrophilicity to the point where it would react with a diazo compound. Thus the reaction of a dihaloalkylborane with a diazo ketone and a diazo ester was briefly studied.

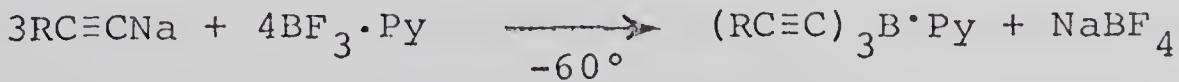


## R E S U L T S    A N D    D I S C U S S I O N

### Reaction of Trialkynylboranes with Ethyl Diazoacetate.

In his report of the synthesis of trialkynylboranes, Ashby notes that these compounds are only obtainable when complexed with such amines as pyridine or diethylamine.<sup>82</sup> Attempts at isolation of the trialkynylboranes from ethereal solutions in the absence of amine stabilizers led to their decomposition. This was characterized by the discolouration of the borane solution, accompanied by the appearance of vinyl absorption in the infrared spectrum of the crude mixture. In general, however, Ashby found that the discolouration (and presumably the decomposition) of the alkynylborane solutions only occurred upon warming these solutions to room temperature. It was thus decided to prepare the trialkynylboranes in a manner analogous to that employed by Ashby but with no attempt at isolation of the product. Instead, the solution would be kept cool and reacted at low temperatures with the desired substrate.

Ashby generated the trialkynylboranes by reacting the desired sodium acetylide salt with boron trifluoride-pyridine using the following stoichiometry.



If this reaction was performed at -30° in tetrahydrofuran a clear, colourless solution resulted. However,



during the course of this investigation it was noted that if this solution was allowed to warm much above 0° it gradually turned a deep brown - very reminiscent of Ashby's observations. As a result, temperatures above 0° were avoided as much as possible.

Trihexynylborane was prepared at -25° by the reaction of hexynyllithium with boron trifluoride-etherate as outlined above. Treatment of the resulting clear, colourless solution with two mole equivalents of ethyl diazoacetate resulted in slow, smooth nitrogen evolution which tapered off at approximately 120% of theory. (A similar observation was made by Linke<sup>100</sup> in the study of the reaction of diazo substrates with trialkylboranes in the presence of water). Workup of the reaction mixture and subsequent investigation by glc showed a yield of 100% of ethyl 3-octynoate based on alkynylborane. Distillation of the crude residue afforded an 85% isolated yield of this ester.

This result indicated the feasibility of the reaction of alkynylboranes with ethyl diazoacetate. In order to assess whether this reaction was generally applicable to a series of acetylenes it was repeated employing triphenylethyneborane. The reaction was again conducted at low temperature but a smaller excess of diazo substrate was employed (1.3:1 of diazoester:borane). This time nitrogen evolution was quantitative and workup of the reaction



mixture allowed isolation of 92% ethyl-4-phenyl-3-butynoate.

In order to investigate whether only one alkynyl group per borane molecule was being efficiently utilized, the reaction of trihexynylborane with ethyl diazoacetate was repeated employing a large excess of diazo compound (3:1 diazo compound: borane). Nitrogen evolution at -20° was slow and smooth but tapered off at 19% (based on diazo compound). The reaction mixture was then warmed to 25° and nitrogen evolution then became quantitative but the reaction discoloured to a deep amber. Workup and investigation of the residue by glc indicated a yield of only 19% of ethyl 3-hexynoate (based on diazo compound). This is equivalent to a 57% yield based on the borane. This figure compares remarkably well with the amount of nitrogen evolution at the time the reaction tapered off at -20° (19% based on diazo compound or 57% based on borane). It would thus seem that the nitrogen evolved upon warming of the reaction mixture to 25° was not the result of conversion of the diazo ester to the desired propargylic ester. It would also appear that, similar to many organoborane reactions, only one alkynyl group per borane is utilized effectively.

The next reaction investigated was that of triheptynylborane with ethyl diazoacetate. Reaction of a slight excess (1.3:1) of diazo substrate with the borane at -20° resulted



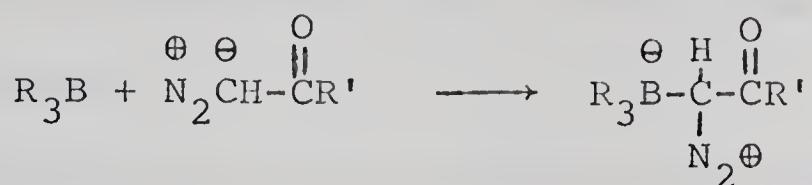
in a tapering off of the reaction after about 100% nitrogen evolution. The reaction was warmed to 0° and nitrogen evolution increased to 164%. This was, however, accompanied by deep colouration of the reaction mixture. Glc analysis showed a 63% yield of the propargylic ester, ethyl 3-nonyoate. Again it appeared that although higher temperature increased the amount of N<sub>2</sub> evolution it did not afford higher yields of desired product.

The reaction was repeated, and again the nitrogen evolution stabilized at about 100% at -20°. Addition of 2 drops of water at this point resulted in a rapid evolution of the remainder of the theoretical quantity of nitrogen accompanied by an exothermic reaction. Glc analysis indicated a 97% yield of ethyl 3-nonyoate.

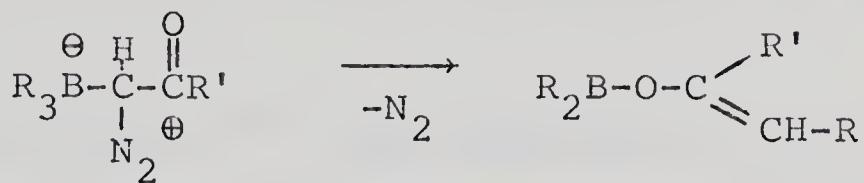
The addition of water to organoborane-diazo compound reactions has been employed in the past to increase the yields of the desired products. Morrison employed water *in situ* in the reaction of trialkylboranes with diazo-acetaldehyde.<sup>83</sup> (He found that higher yields of the homologated aldehyde product were obtained and suggested that the intermediate involved in the reaction was hydrolysed before it could be consumed by some undesirable side reaction). It is difficult to explain, though, why, in the present case, the presence of water should have any effect on nitrogen evolution. The mechanism currently proposed for the borane-diazo compound reaction involves



the reaction of the borane with the diazo substrate to form a Lewis acid-base pair.



Then an intramolecular rearrangement takes place involving an alkyl group migration and expulsion of nitrogen to give an enol borinate (vinyloxyborane) intermediate possibly *via* a species of the type  $R_2B\begin{matrix} \overset{R}{|} \\ -CH-C(=O)-R' \end{matrix}$



These vinyloxyboranes have been isolated by Pasto and coworkers<sup>101,102</sup>, and postulated as intermediates in the conjugate addition of trialkylboranes to  $\alpha,\beta$ -unsaturated ketones<sup>46</sup> and aldehydes<sup>47</sup> by Brown and coworkers. Any water present will hydrolyse the enol borinate giving rise to the desired product and a borinic acid.

Consequently a trialkynylborane was reacted with ethyl diazoacetate in the presence of water to assess what effect, if any, this would have on the reaction. Tripentynylborane was the borane chosen. At  $-19^{\circ}$  nitrogen evolution was rapid and smooth. After 0.84 hr quantitative nitrogen evolution indicated completion of reaction. However, glc analysis indicated a yield of only 63% of the



propargylic ester, ethyl 3-heptynoate. Thus, although the presence of water rapidly accelerated the reaction, it did not increase the yield of the desired product by any great degree.

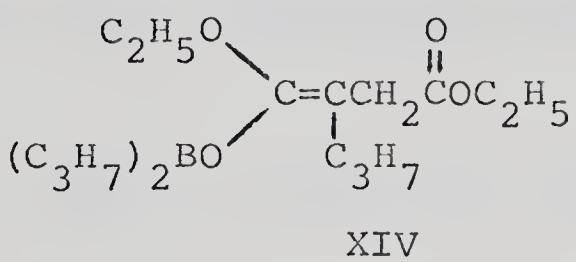
The reaction was repeated in the absence of water. After 1.25 hr nitrogen evolution had stabilized at 43%. Addition of 2 drops of water at this point caused an acceleration in the evolution of nitrogen and after another 0.25 hr 83% of theory had been evolved. The reaction was worked up and 65% of ethyl 3-heptynoate was detected by glc.

Hooz and Gunn <sup>103</sup> have employed a ratio of 1.5:1 of organoborane: ethyl diazoacetate to obtain nearly quantitative yields of the corresponding homologated esters. All experiments conducted in this study had employed excess diazo compound. In order to assess the effect of decreasing the excess of diazoester present, the reaction of ethyl diazoacetate with tripentynylborane was repeated using a ratio of 1:1.05. After 2.5 hr at -20° nitrogen evolution had stabilized at 86% of theory. Addition of 1 ml of water and stirring for 3 hr caused the nitrogen evolution to become quantitative. Workup of the reaction mixture and analysis of the residue by glc indicated a yield of 37% of ethyl 3-heptynoate.

This low yield of propargylic ester, coupled with the results from the previous experiments, indicate the



necessity of having an excess of diazo compound present for the trialkynylborane-diazoester reaction mixture. It would also seem that some side reaction takes place, consuming the diazo substrate before it can react with the alkynylborane to lead to propargylic ester. Hooz and Linke<sup>81</sup> report that some undetermined side reaction consumes ethyl diazoacetate in their reactions of various trialkylboranes with this diazo substrate. Pasto and co-workers<sup>101</sup> report a byproduct (XIV) isolated in their study of the intermediates involved in the reaction of tri-*n*-propylborane with ethyl diazoacetate:



This product presumably arises from reaction of the vinyloxyborane intermediate with another molecule of ethyl diazoacetate and thus could explain the additional consumption of the diazo ester. (No attempts were made in the present study, however, to determine the nature or extent of this side reaction).

In fact, if the reaction of tripentynylborane with ethyl diazoacetate is repeated using a large excess of diazo ester (2:1 ester to borane), a 71% yield of the propargylic ester, ethyl 3-heptynoate, is obtained.



It has been established that only one "ligand" of the trialkynylborane was being efficiently utilized in the reaction with ethyl diazoacetate. In an attempt to circumvent this problem it was decided to prepare a "mixed" organoborane (analogous to the "mixed" dialkyl-alkynylalane prepared in Chapter II) and investigate its reaction with ethyl diazoacetate.

Dialkylalkynylboranes have been synthesized by many workers but the majority were prepared as their pyridine-complexed forms.<sup>104,105</sup> Lappert and Prokai<sup>106</sup> have prepared the uncomplexed "mixed" organoborane, diphenylphenylethyneborane, by reaction of diphenylboron chloride with the lithium salt of phenylacetylene:



The chemistry of the product was only briefly investigated. Lappert and Prokai found that HBr, rather than add to the triple bond, cleaved the B-C bond to give mixture of  $\Phi_2^{\circ} \text{BBr}$ ,  $\Phi \text{BBr}$ , and  $\alpha$ -bromostyrene..

Dibutylheptynylborane was prepared in a fashion analogous to that employed by Lappert and Prokai - reaction of lithium hexynide with a dibutylboron halide. To obtain the desired halo organoborane, the procedure of Johnson, Snyder and Van Campen<sup>107</sup> was employed. They found that reaction of anhydrous HBr with tri-*n*-butylbor-



ane at 55 - 60° resulted in the formation of one mole of *n*-butane, and di-*n*-butylboron bromide was isolated in almost quantitative yield. The reaction of HBr with commercially available tri-*n*-butylborane was conducted under identical conditions to those employed by Johnson and coworkers and afforded di-*n*-butylboron bromide in 75% yield. The percentage of bromine in the borane was determined by hydrolysing aliquots and titrating the bromide ion with silver nitrate. This analysis showed one bromine atom per borane molecule. In addition, the borane was oxidized with *meta*-chloroperbenzoic acid <sup>108</sup> and the amount of *n*-butanol formed was determined by glc. This oxidation showed two butyl groups present per borane molecule.

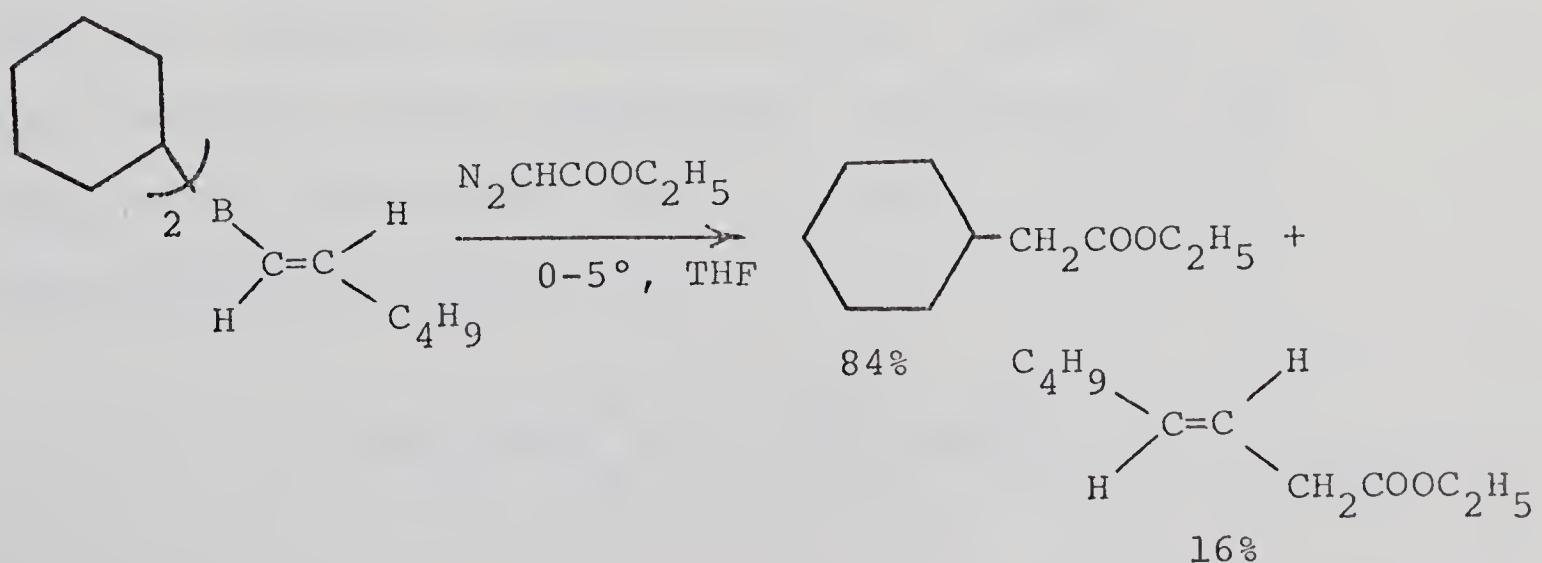
With the purity of the dibutylbromoborane established, the next step was to form the "mixed", dialkylalkynylborane. Equimolar amounts of dibutylboron bromide and lithium heptynide were reacted at -20° in pentane (to facilitate the precipitation of LiBr). After reaction for 1 hr at -20° and decantation from the precipitated LiBr, THF was added to the supernatant. The resultant solution was reacted with ethyl diazoacetate and after reaction for 4 hr at -20°, nitrogen evolution was only 30% of theory. (Addition of water at this point caused no further evolution of gas and infrared analysis showed considerable diazo absorption at 2000 cm<sup>-1</sup>). Glc analysis



showed no trace of the propargylic ester, ethyl 3-octynoate. However, 34% of ethyl hexanoate was detected (by comparison with an authentic sample).

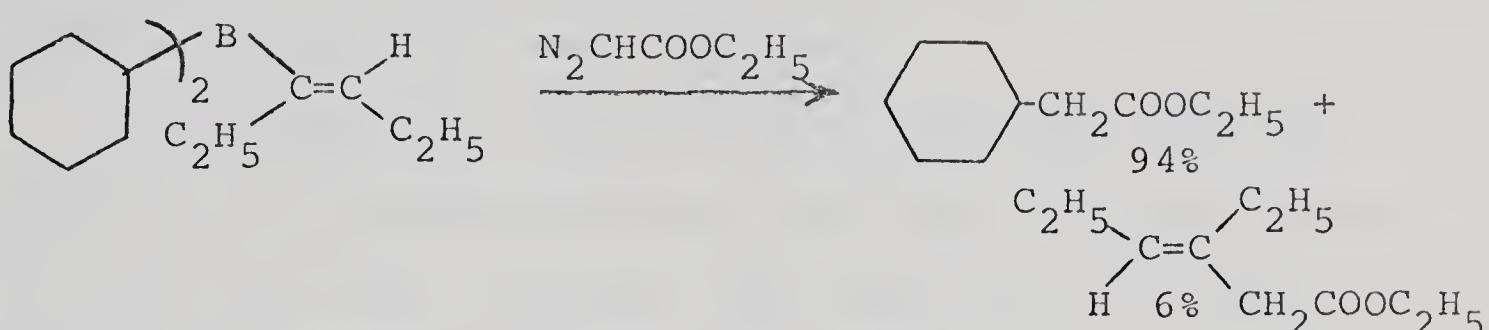
These results indicated a preferential migration of the butyl "ligand" attached to boron over the hexynyl moiety. To account for the remainder of the butyl groups the reaction mixture was oxidized with *meta*-chloroperbenzoic acid (thus converting any remaining boron-bound butyl groups to *n*-butanol). Analysis by glc indicated 71% of *n*-butanol present.

This preferential migration of the ligand with the greatest degree of "p"-character is not without precedent in the reactions of "mixed" organoboranes with diazo substrates. When dicyclohexylhexenylborane is reacted with ethyl diazoacetate, 84% of the ester product is ethyl cyclohexylacetate and only 16% is ethyl 3-octenoate<sup>109</sup> (the total ester yield being 72%) *viz.*





In addition, the reaction of dicyclohexylhex-3-enylborane with ethyl diazoacetate gives 94% ethyl cyclohexylacetate and only 6% ethyl 3-ethyl-3-hexenoate (the total ester yield being 56%).<sup>109</sup>



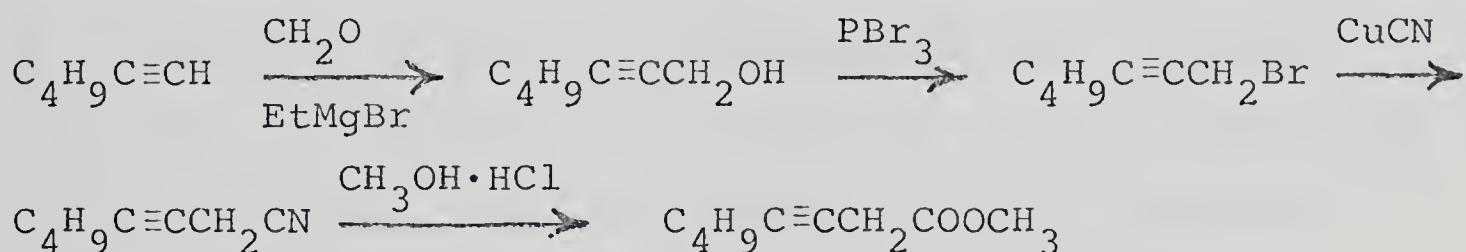
Parsons and coworkers<sup>110</sup> have shown that the presence of a vinyl or propenyl group in an organoborane stabilizes it relative to its alkyl-substituted counterpart. They have shown that dimethylvinylboron will decompose by 33% when kept at room temperature for five days. If a second vinyl group is introduced it tends to stabilize the compound and thus divinylmethylborane remains almost unchanged when heated to 100° for 1 hr and only decomposes slightly when heated at 100° for 70 hr. They reason that the increased stability of these compounds is due to a mesomeric effect whereby the π electrons of the vinyl group are donated into the vacant p orbital of the neighbouring boron atom:





This effect might also explain why an alkyl group bonded to boron would migrate preferentially over an alkenyl (or alkynyl) group in a "mixed" organoborane. Presumably the mesomeric effect would serve to strengthen the bond between the  $\text{sp}^2$  (or  $\text{sp}$ )-hybridized carbon atom to boron and thus make the migration of this unsaturated ligand energetically less favourable.

The propargylic ester products obtained from the reaction of a trialkynylborane with ethyl diazoacetate as outlined above are otherwise only available by rather circuitous procedures. Newman and Wotiz<sup>111</sup> have synthesized methyl 3-octynoate from 1-hexyne using classical techniques *viz.*



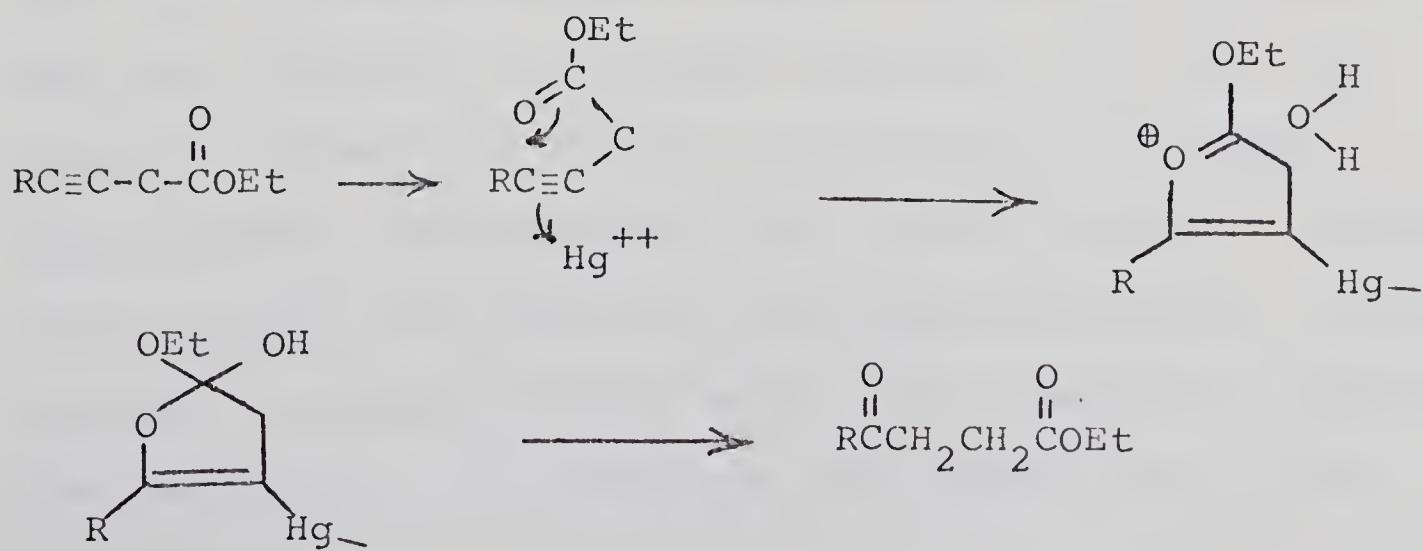
The overall yield obtained in converting 1-hexyne to the methyl ester of 3-octynoic acid was 40%. The yield of the ethyl ester of 3-octynoic acid from 1-hexyne *via* the trihexynylborane reagent was 82%. Craig and Moyle<sup>112</sup> found that C<sub>5</sub> to C<sub>9</sub>  $\alpha,\beta$ -acetylenic acids could be transformed to their  $\beta,\gamma$ -isomers by treatment with sodamide in liquid ammonia. The product mixture contains 80 - 95% of the  $\beta,\gamma$ -acetylenic isomer. The method,



however, suffers from lack of general applicability and contamination of the product with the  $\alpha, \beta, \gamma$ -allenic isomer.

Having established an efficient method for the synthesis of  $\beta, \gamma$ -acetylenic esters we next investigated their chemical behaviour. In particular, we were interested in establishing whether or not the triple bond could be hydrated preferentially in either direction. Addition of hydroxyl at the carbon  $\beta$  to the carbethoxy group would afford  $\beta$ -keto esters while addition  $\gamma$  to the carbethoxyl would provide  $\gamma$ -keto esters. Both these types of esters are synthetically valuable.

Ethyl 3-heptynoate was refluxed with dilute acid and mercuric sulfate overnight under nitrogen. Upon work-up a 91% yield of ethyl 4-oxoheptanoate was obtained. There was no evidence for the formation of the corresponding  $\beta$ -keto ester. This regiospecificity of hydration can be rationalized if we consider an intermediate similar to the one proposed by Stork and Borch for the hydration of  $\gamma, \delta$ -acetylenic ketones.<sup>26</sup> Thus:





To establish that this hydration phenomenon was generally applicable to  $\beta,\gamma$ -acetylenic esters the other propargylic esters obtained in this study were subjected to similar hydration conditions. In this manner ethyl 3-nonynoate was hydrated to ethyl 4-oxononanoate in 83% isolated yield, ethyl 3-octynoate to ethyl 4-oxooctanoate in 82% isolated yield, and ethyl 4-phenyl-3-butynoate to ethyl 3-phenacylpropionate in 61% isolated yield.

Reaction of Phenylboron Dichloride with Ethyl Diazoacetate and a Diazoketone.

In an attempt to circumvent the loss of 66% of the alkyl groups bound to boron in the reaction of a trialkylborane with a diazo substrate, the reactions of an alkyldihaloborane with a representative diazoester and diazoketone were investigated. Phenylboron dichloride was chosen as the borane because it was commercially available.

Reaction of ethyl diazoacetate with an equimolar amount of phenylboron dichloride at 15° in diethyl ether led to a rapid and quantitative evolution of nitrogen. Upon the cessation of nitrogen evolution (0.5 hr), the reaction mixture was worked up but only 14% of ethyl phenylacetate was detected in the residue by glc. Because of the vigour with which the nitrogen was evolved, it was decided to attenuate the reaction rate somewhat by reducing the temperature. The reaction was repeated at -25° in



diethyl ether. This time, however, a 2:1 equivalence of diazoester to borane was employed. The reaction again proceeded smoothly and nitrogen evolution was rapid. After 1.5 hr the nitrogen evolution was 92% based on diazo substrate (184% based on organoborane) and the reaction mixture was worked up. Analysis of the residue by glc indicated a yield of 21% of ethyl phenylacetate.

The reaction still appeared to be too violent. In order to further attenuate the reactivity of the organoborane, a stronger Lewis base was chosen as solvent. The reaction was repeated again in tetrahydrofuran. Again a 2:1 equivalence of diazo compound to organoborane was employed and again the reaction was conducted at low temperature (-27°). Nitrogen evolution was now much slower but smooth and after 2.5 hr had stabilized at 49% of theory, based on diazo ester (98% based on organoborane). Workup of the reaction mixture and analysis of the residue by glc indicated a yield of 100% of ethyl phenylacetate.

These results indicate that high temperature increases the rate of decomposition of diazo compound without significantly increasing the amount of desired product. In addition, the use of THF as a solvent seems to inhibit this non-constructive decomposition of diazo substrate.

With these facts in hand, phenylboron dichloride was reacted with a diazoketone (diazoacetophenone). Equimolar quantities of each reactant were employed in THF at -25°.



Nitrogen evolution was smooth and rapid and quantitative after 2 hr. Workup of the reaction mixture and analysis of the residue by glc indicated only 35% of the desired product, deoxybenzoin.

Alkylboron dichlorides are unstable in the presence of water, giving rise to boronic acids and HCl. This fact precludes the possibility of performing the above reactions in the presence of water in an attempt to improve yields of the desired products. However, the reaction of phenylboron dichloride with ethyl diazoacetate gives encouragement to the idea that alkylboron dihalides can be used to circumvent the loss of alkyl groups in borane-diazo substrate reactions.



EXPERIMENTALGeneral Considerations.

Infrared (ir) spectra were recorded using a Perkin-Elmer 337G, Perkin-Elmer 421G or Unicam SP 1000 Infrared Spectrophotometer.

Nuclear magnetic resonance (nmr) spectra were recorded on a Varian A-60 or HR-100 Spectrometer. Unless otherwise stated deuteriochloroform ( $\text{CDCl}_3$ ) was employed as the solvent with tetramethylsilane (TMS) as the internal reference. Chemical shifts are reported as  $\tau$  values relative to TMS = 10. The following abbreviations are used in the text: s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet.

Mass spectra were recorded on an AEI Model MS-2 or Model MS-9 Spectrometer. Spectra are recorded in the following fashion: m/e: peak mass (relative intensity).

Gas liquid chromatography (glc) was performed using an Aerograph A-90-P3 and a Varian Aerograph Series 1200 chromatograph.

Refractive indices were measured on a Bausch and Lomb Abbé -3L Refractometer.

Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected.

Typical Preparation of an Alkynylborane.

All operations were carried out under an atmosphere



of purified nitrogen. A solution of *n*-butyllithium in hexane<sup>21</sup> (40 mmole) was slowly added to a solution of alkyne (40 mmole) in THF (35 ml) at -20°. The resultant solution was stirred at -20° for 0.5 hr and then boron trifluoride-etherate (54 mmole) was added slowly, maintaining the temperature below -15°. The resultant clear, colourless solution was stirred at -20° for 0.5 hr. The apparatus was then connected to an azotometer and the alkynylborane was ready for reaction with the diazoester.

Typical Workup of Trialkynylborane - Ethyl Diazoacetate Reaction Mixture.

The trialkynylborane-ethyl diazoacetate reaction mixture was stirred until the nitrogen evolution stabilized. The reaction mixture was then quenched by pouring into ice water (200 ml) and stirring for 0.5 hr. The two layers were separated and the aqueous phase was extracted (3 x 30 ml) with ether. The combined organic phase was dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated *in vacuo* to afford the crude product mixture as an oil.

Reaction of Trihexynylborane with Ethyl Diazoacetate.

A solution of trihexynylborane (10 mmole) in THF (40 ml) was prepared as described above from 1-hexyne (4.3 ml; 30 mmole). Ethyl diazoacetate (2.19 g; 19 mmole) in THF (20 ml) was slowly added to the above solution maintaining the temperature below -15° and monitoring the gas evolution



with an azotometer. After stirring at this temperature for 6.5 hr the reaction's evolution of nitrogen had stabilized at 310 ml (60% of theoretical, based on diazo-ester). The reaction was worked up as described above and the oily residue so obtained was found to contain 100% of ethyl 3-octynoate by glc (15% FFAP; 165°). The oil was subjected to vacuum distillation and afforded 1.42 g (88%) of the propargylic ester, bp 80-83° (3 mm),  $n_D^{26} = 1.4410$ . ir (liquid film)  $1740\text{ cm}^{-1}$  (ester C=O); nmr:  $\tau$  5.80 (q,2)  $\text{OCH}_2-\text{CH}_3$ , 6.77 (t,2)  $\text{CH}_2\text{C}\equiv\text{C}-\text{CH}_2$ , 7.80 (m,2)  $\text{CH}_2\text{CH}_2\text{C}\equiv\text{C}$ , 8.70 (t,3)  $\text{CH}_3\text{CH}_2-\text{O}$ , 8.20 - 8.80 (m,4)  $\text{CH}_2\text{CH}_2$ , 9.10 (t,3)  $\text{CH}_3\text{CH}_2$ ; mass spectrum  $m/e$ : 168(0.27), 139(7), 126(23), 98(20), 95(26), 81(17), 79(14), 67(63), 55(31), 54(24), 53(31), 41(30), 29(100). Anal. Calcd. for  $\text{C}_{10}\text{H}_{16}\text{O}_2$ : C, 71.39; H, 9.59. Found. C, 70.90; H, 9.42.

#### Reaction of Triphenylethylnylborane with Ethyl Diazoacetate.

A solution of triphenylethylnylborane (10 mmole) in THF (40 ml) was prepared as described above from phenyl-acetylene (3.06 g; 30 mmole). Ethyl diazoacetate (1.46 g; 12.8 mmole) in THF (20 ml) was slowly added to the above solution maintaining the temperature below -15° and monitoring the gas evolution with an azotometer. After stirring at this temperature for 1.25 hr, gas evolution was quantitative (based on diazo ester) and the reaction was worked up as described above. The crude residue so obtained



was subjected to vacuum distillation and afforded 1.72 g (92%) ethyl 4-phenyl-3-butynoate, bp 122-124° (2.5 mm)  $n_D^{26} = 1.5208$ . ir (liquid film) 1735 (ester C=O), 3060, 1490, 1440, 760  $\text{cm}^{-1}$  ( $\text{C}_6\text{H}_5$ ); nmr  $\tau$ : 8.61 (m,5)  $\text{C}_6\text{H}_5-$ , 5.79 (q,2)  $\text{OCH}_2\text{CH}_3$ , 4.50 (s,2)  $\phi\text{C}\equiv\text{C}-\text{CH}_2$  2.75 (t,3)  $\text{CH}_3\text{CH}_2\text{O}$ ; mass spectrum m/e: 188(38), 160(10), 144(9), 129(8), 116(26), 115(100), 89(14), 63(14), 29(60).

Reaction of Trihexynylborane with Ethyl Diazoacetate in a 1:3 Ratio.

A solution of trihexynylborane (5 mmole) in THF (30 ml) was prepared as described above from 1-hexyne (1.5 ml; 15 mmole). Ethyl diazoacetate (2.19 g; 15 mmole) in THF (20 ml) was added slowly maintaining the temperature at -20°. Nitrogen evolution was measured with an azotometer. The evolution was slow and stabilized after 100 ml (20% based on diazo ester) had been evolved. The reaction mixture was allowed to warm to room temperature overnight and nitrogen evolution was then 530 ml (100% of theory based on diazo ester). The deep amber reaction mixture was worked up as described above and the residue was made up to 50 ml in a volumetric flask. Analysis of this solution by glc (10% FFAP; 155°) indicated a yield of 19% (based on diazo ester) of ethyl 3-octynoate. A



sample was isolated by preparative glc (10% FFAP; 160°) and was shown to be identical with the compound obtained on pg 147.

Reaction of Triheptynylborane with Ethyl Diazoacetate.

A solution of triheptynylborane (10 mmole) in THF (30 ml) was prepared as described above from 1-heptyne (2.88 g; 30 mmole). Ethyl diazoacetate (1.46 g; 12.8 mmole) in THF (10 ml) was slowly added, maintaining the temperature below -20°. Nitrogen evolution was slow and smooth and monitored with an azotometer. After 0.5 hr the gas evolution had stabilized at 170 ml (48% theoretical based on diazo ester) and the reaction mixture was warmed to 0°. The reaction mixture took on an amber colouration and after stirring at this temperature for 1 hr nitrogen evolution stabilized at 290 ml (82% of theory, based on diazo ester). The reaction mixture was worked up as described above. Examination of the crude residue by glc (10% FFAP; 180°) indicated a yield of 63% ethyl 3-nonynoate. The residue was subjected to vacuum distillation and afforded 0.59 g (47%) ethyl 3-nonynoate, bp 86 -87° (1.5 mm),  $n_D^{22} = 1.4440$ . ir (liquid film)  $1735\text{ cm}^{-1}$  (ester C=O); nmr  $\tau$ : 5.75 (q, 2)  $\text{OCH}_2\text{CH}_3$ , 6.70 (t, 2)  $\text{C}\equiv\text{CCH}_2\text{C=O}$ , 7.80 (m, 2)  $\text{CH}_2\text{C}\equiv\text{C}$ , 8.30 - 8.80 (m, 6)  $(\text{CH}_2)_3$ , 8.69 (t, 3)  $\text{CH}_3\text{CH}_2\text{O}$ , 9.09 (t, 3)  $\text{CH}_3\text{CH}_2^-$ ; mass spectrum  $m/e$ : 182(0.15), 155(3.0), 126(6.0), 108(34), 98(16), 95(15),



67(75), 55(35), 41(38), 29(100). Anal. Calcd. for  $C_{11}H_{18}O_2$ : C, 72.49; H, 9.95. Found: C, 72.52; H, 9.76.

Reaction of Triheptynylborane with Ethyl Diazoacetate.

Triheptynylborane (10 mmole) in THF (40 ml) was prepared as described above from 1-heptyne (2.88 g; 30 mmole). Ethyl diazoacetate (1.46 g; 12.8 mmole) in THF (15 ml) was slowly added, maintaining the temperature below  $-20^\circ$ . Nitrogen evolution was monitored with an azotometer. After stirring at this temperature for 1.5 hr, gas evolution had stabilized at 150 ml (42% based on diazo ester). Addition of 2 drops of water caused a vigorous evolution of nitrogen accompanied by a rise in temperature to  $-12^\circ$ . After stirring a further 20 minutes, nitrogen evolution was 355 ml (100% based on diazo ester). Workup of the reaction mixture as described above afforded a pale yellow oil. Analysis of the oil by glc (15% FFAP;  $180^\circ$ ) showed 97% yield of ethyl 3-nonynoate. The residue was subjected to vacuum distillation and afforded 1.44 g (87%) ethyl 3-nonynoate, bp 90 - 91 $^\circ$  (2.5 mm), identical in all respects to the compound obtained from the above reaction.

Reaction of Tripentynylborane with Ethyl Diazoacetate  
in the Presence of Water.

Tripentynylborane (13 mmole) in THF (40 ml) was prepared as described above from 1-pentyne (2.72 g; 40



mmole). While maintaining the temperature below -20°, water (0.5 cc; 28 mmole) was added. Ethyl diazoacetate (1.94 g; 17.5 mmole) in THF (15 ml) was then slowly added and the temperature was not allowed to rise above -19°. Nitrogen evolution, monitored by an azotometer, was rapid and smooth. After stirring at this temperature for 50 minutes, nitrogen evolution was 485 ml (100% based on diazo ester). The reaction mixture was worked up as described above and the yield of ethyl 3-heptynoate in the residue so obtained was estimated as 63% by glc (10% FFAP; 170°). The residue was subjected to vacuum distillation and afforded 1.09 g (51%) ethyl 3-heptynoate, bp 78 - 79° (6.5 mm),  $n_D^{21} = 1.4376$ . ir (liquid film). 1735  $\text{cm}^{-1}$  (ester C=O); nmr  $\tau$ : 5.75 (q,2)  $\text{OCH}_2\text{CH}_3$ , 6.71 (t,2)  $\text{CH}_2\text{C}\equiv\text{CCH}_2\text{C=O}$ , 7.80 (m,2)  $\text{CH}_2\text{CH}_2\text{C}\equiv\text{C}$ , 8.55 (m,2)  $\text{CH}_3\text{CH}_2\text{CH}_2$ , 8.71 (t,3)  $\text{CH}_3\text{CH}_2\text{O}$ , 9.01 (t,3)  $\text{CH}_3\text{CH}_2$ ; mass spectrum  $m/e$ : 154(1.1), 126(34), 125(19), 109(10), 95(7), 81(44), 79(25), 67(36), 53(28), 41(27), 29(100). Anal. Calcd. for  $\text{C}_9\text{H}_{14}\text{O}_2$ : C, 70.10; H, 9.15. Found: C, 69.61; H, 9.26.

#### Reaction of Tripentynylborane with Ethyl Diazoacetate.

Tripentynylborane (13 mmole) in THF (40 ml) was prepared as described above from 1-pentyne (2.72 g; 40 mmole). Ethyl diazoacetate (1.94 g; 17.5 mmole) in THF (15 ml) was then slowly added, keeping the temperature below -19°. Nitrogen evolution was monitored by an azo-



tometer and after 1.25 hr was observed to stabilize at 210 ml (43% based on diazo ester). Addition of 2 drops of water at this point caused a resumption of the evolution of nitrogen and an increase in the temperature of reaction to -10°. After stirring a further 0.25 hr, nitrogen evolution was quantitative. The reaction mixture was worked up as described above and glc analysis (10% FFAP; 180°) of the residue indicated a 65% yield of ethyl 3-heptynoate. The residue was subjected to vacuum distillation and afforded 1.46 g (63%) of the propargylic ester, bp 78 - 80° (8 mm), identical in all respects to the compound obtained above.

Reaction of Tripentynylborane with Ethyl Diazoacetate in a 1.05:1 Ratio.

Tripentynylborane (7 mmole) in THF (30 ml) was prepared as described above from 1-pentyne (1.56 g: 21 mmole). Ethyl diazoacetate (0.84 g; 7.4 mmole) in THF (10 ml) was slowly added maintaining the reaction temperature below -20°. Nitrogen evolution was monitored with an azotometer and after 2.5 hr was observed to stabilize at 160 ml (86% based on diazo ester). Water (1 ml; 56 mmole) was added and after stirring a further 3 hr nitrogen evolution was quantitative (185 ml). The reaction mixture was worked up as described above and glc analysis (10% FFAP; 160°) of the residue indicated a yield of 37% of ethyl 3-heptynoate.



A small sample was isolated by preparative glc (15% FFAP; 170°) and proved to be identical with the compound obtained above.

Reaction of Tripentynylborane with Ethyl Diazoacetate in a 1:2 Ratio.

Tripentynylborane (20 mmole) in THF (30 ml) was prepared as described above from 1-pentyne (4.08 g; 60 mmole). Ethyl diazoacetate (4.45 g; 40 mmole) in THF (15 ml) was added slowly while the temperature of the reaction mixture was maintained at -19°. Nitrogen evolution was monitored by an azotometer and stabilized at 532 ml (47% based on diazo ester) after 2 hr. The reaction mixture was worked up as described above. The yield of ethyl 3-heptynoate in the crude residue was determined as 71% by glc (10% FFAP; 150°). The residue was subjected to vacuum distillation and afforded 1.49 g (47%) propargylic ester, bp 81 - 82° (8 mm), identical in all respects to the compound obtained above.

Preparation of Dibutylboran Bromide.

Dibutylboron bromide was prepared by treatment of commercially available tri-*n*-butylborane<sup>113</sup> with anhydrous HBr at 55 - 60° according to the method of Johnson, Snyder and Van Campen.<sup>107</sup> The colourless oil, bp 82 - 85° (16 mm) [lit<sup>106</sup> 44° (4 mm)], was obtained in 75% yield.



The compound was analysed for bromine by hydrolysis of aliquots in distilled water and titration with silver nitrate <sup>114</sup> and found to contain one mole bromine per mole of borane.

In order to estimate the number of butyl groups bound to boron, aliquots of the bromoborane were oxidized with *meta*-chloroperbenzoic acid according to the method of Johnson and Van Campen.<sup>97</sup> Analysis by glc (10% FFAP; 80°) of the butanol formed showed two butyl groups per borane molecule bound to boron.

Reaction of Dibutylhexynylborane with Ethyl Diazoacetate.

1-Heptyne (.96 g; 10 mmole) in pentane (20 ml) was converted to its lithium salt by the addition of a solution of *n*-butyllithium in hexane <sup>21</sup> (10 mmole). The resultant gelatinous suspension was cooled to -20° and ether (5 ml) was added. Dibutylboron bromide (2.08 g; 10 mmole) in a pentane:THF solvent (5 ml 1:1 by volume) was slowly added (exothermic). The resultant mixture was diluted with pentane (10 ml) and stirred for 0.75 hr. The precipitated white solid was allowed to settle and the clear supernatant decanted, maintaining the temperature below -20°. The reaction mixture was concentrated *in vacuo* and then diluted with THF (40 ml) at -20°. Ethyl diazoacetate (1.46 g; 13 mmole) in THF (10 ml) was slowly added maintaining the temperature at -20°. Nitrogen evolution was



monitored with an azotometer and after 4 hr had stabilized at 120 ml (30%). Addition of water (2 ml; 112 mmole) caused no change in the nitrogen evolution. Examination of an aliquot of reaction mixture by infrared showed considerable diazoester still present. The reaction mixture was poured into distilled water and the organic layer was separated. The aqueous layer was extracted with ether (2 x 15 ml) and the combined organic phase was dried ( $\text{Na}_2\text{SO}_4$ ), concentrated *in vacuo* and made up to 50 ml in a volumetric flask. Analysis of the crude reaction mixture by glc (10% FFAP; 180°) showed complete absence of ethyl 3-nonyoate. The yield of ethyl hexanoate was determined as 34% by glc (10% FFAP; 90°).

The remainder of the reaction mixture was oxidized with *meta*-chloroperbenzoic acid according to Johnson and Van Campen<sup>108</sup> and the yield of *n*-butanol was estimated as 71% by glc (10% FFAP; 70°).

#### Hydration of Ethyl 3-Octynoate.

Ethyl 3-octynoate (700 mg; 4 mmole) in 98% ethanol (25 ml) was refluxed with water (7 ml), sulfuric acid (2 drops) and mercuric sulfate (15 mg) for 12 hr. The solvent was evaporated and the oily residue taken up with ether. The ethereal solution was washed with saturated sodium bicarbonate, dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated. The residue was subjected to molecular distillation and



afforded 634 mg (82%) ethyl 4-oxooctanoate  $n_D^{20} = 1.4338$  (lit  $^{115} n_D^{20} = 1.4340$ ). ir (liquid film) 1710 (C=O), 1735  $\text{cm}^{-1}$  (shoulder, ester C=O); nmr  $\tau$ : 5.85 (q, 2)  $\text{OCH}_2\text{CH}_3$ , 7.40 (m, 6)  $\text{CH}_2\overset{\text{O}}{\underset{\text{C}}{\text{C}}}$ , and  $\text{CH}_2\overset{\text{O}}{\underset{\text{C}}{\text{CH}_2\text{COEt}}}$ , 8.56 (m, 4)  $\text{CH}_3\text{CH}_2\text{CH}_2$ , 8.74 (t, 3)  $\text{CH}_3\text{CH}_2\text{O}$ , 9.06 (t, 3)  $\text{CH}_3\text{CH}_2\text{CH}_2$ ; mass spectrum (calcd. for  $\text{C}_{10}\text{H}_{18}\text{O}_3$ : 186.1256; found: 186.1255).  $m/e$ : 186(0.36), 157(1.5), 144(76), 141(70), 129(32), 111(15), 101(100), 98(93), 85(90), 57(85), 29(55).

#### Hydration of Ethyl 3-Nonyoate

Ethyl 3-nonyoate (1.11 g; 5.6 mmole) in 98% ethanol (50 ml) was refluxed with water (10 ml) sulfuric acid (3 drops) and mercuric sulfate (10 mg) for 5 hr. The solvent was evaporated and the oily residue taken up with ether. The ethereal solution was washed with saturated sodium bicarbonate, dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated. The residue was subjected to molecular distillation and afforded 1.00 g (85%) ethyl 4-oxononanoate  $n_D^{21} = 1.4369$  (lit  $^{115} n_D^{20} = 1.4367$ ). ir (liquid film) 1735 (ester C=O), 1710  $\text{cm}^{-1}$  (shoulder C=O). nmr  $\tau$ : 5.88 (q, 2)  $\text{OCH}_2\text{CH}_3$ , 7.41 (m, 6)  $\text{CH}_2\overset{\text{O}}{\underset{\text{C}}{\text{C}}}\text{CH}_2\overset{\text{O}}{\underset{\text{C}}{\text{CH}_2}}$ , 8.65 (m, 6)  $(\text{CH}_2)_3$ , 8.75 (t, 3)  $\text{CH}_3\text{CH}_2\text{O}$ , 9.11 (t, 3)  $\text{CH}_3\text{CH}_2$ ; mass spectrum  $m/e$ : 189(0.01), 156(45), 144(6), 129(28), 111(19), 101(80), 99(60), 98(100), 71(50), 56(20), 55(25), 43(91), 41(30), 29(50).



Hydration of Ethyl 3-Heptynoate.

Ethyl 3-heptynoate (1.00 g; 6.5 mmole) in 98% ethanol (50 ml) was refluxed with water (5 ml), sulfuric acid (2 drops) and mercuric sulfate (20 mg) under nitrogen for 12 hr. The solvent was evaporated and the oily residue was taken up in ether. The ethereal solution was washed with saturated sodium bicarbonate, dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated. Distillation of the residue gave 1.06 g (91%) ethyl 4-oxoheptanoate, bp  $63 - 65^\circ$  (0.75 mm) [lit <sup>116</sup>  $83^\circ$  (3 mm)]  $n_D^{20} = 1.4314$  (lit <sup>115</sup>  $n_D^{20} = 1.4312$ ). ir (liquid film) 1735 (shoulder ester C=O),  $1710 \text{ cm}^{-1}$  (C=O); nmr  $\tau$ : 5.85 (q, 2)  $\text{OCH}_2\text{CH}_3$ , 7.50 (m, 6)  $\text{CH}_2\text{CH}_2\text{C=O}$ , and  $\text{O=CCH}_2\text{CH}_2\text{CO}$ , 8.40 (m, 2)  $\text{CH}_3\text{CH}_2\text{CH}_2$ , 8.75 (t, 3)  $\text{CH}_3\text{CH}_2\text{O}$ , 9.10 (t, 3)  $\text{CH}_3\text{CH}_2\text{CH}_2$ ; mass spectrum m/e: 172(6.5), 144(25), 129(36), 127(56), 101(86), 71(100), 55(21), 43(75).

Hydration of Ethyl 4-Phenyl-3-butynoate

Ethyl 4-phenyl-3-butynoate (900 mg; 5.3 mmole) in 98% ethanol (30 ml) was refluxed with water (1 ml), sulfuric acid (2 drops) and mercuric sulfate (5 mg) for 1 hr. The reaction mixture rapidly took on a deep pink colouration. The solvent was evaporated and the red, oily residue was taken up in ether. The ethereal solution was washed with saturated sodium bicarbonate, dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated. The red residue was subjected to molecular distillation and afforded 600 mg (61%) ethyl 3-phenacylpropionate,  $n_D^{22} = 1.5185$



(lit  $^{116}n_D^{20} = 1.5196$ ). ir (thin film) 1735 (ester C=O), 1690 (ArC=O), 1590, 1450, 750, 690  $\text{cm}^{-1}$  (Ar); nmr  $\tau$ : 1.80-2.60 (m,5)  $\text{C}_6\text{H}_5-$ , 5.82 (q,2)  $\text{CH}_2\text{CH}_3$ , 6.70 (t,2)  $\text{CCH}_2\text{CH}_2\text{COEt}$ , 7.26 (t,2)  $\text{CH}_2\text{CH}_2\overset{\text{O}}{\text{COEt}}$ , 8.76 (t,3)  $\text{CH}_3\text{CH}_2\text{O}$ ; mass spectrum  $m/e$ : 208(11), 161(21), 133(4), 105(100), 76(32), 51(12), 29(7), 28(10).

Reaction of Phenylboron Dichloride with Ethyl Diazoacetate  
in Diethyl Ether.

To a solution of phenylboron dichloride <sup>21</sup> (3.18 g; 20 mmole), dissolved in ether (30 ml) was slowly added a solution of ethyl diazoacetate (2.28 g; 20 mmole) in ether (20 ml) while maintaining the temperature at 15°. Nitrogen evolution was measured with an azotometer and was rapid and smooth. After 0.5 hr nitrogen evolution was quantitative and the reaction mixture was poured into dilute (~2N) sodium hydroxide solution. After stirring for 20 minutes the two layers were separated and the aqueous phase extracted with ether (3 x 30 ml). The combined organic phase was dried ( $\text{Na}_2\text{CO}_3$ ), and evaporated. The yield of ethyl phenylacetate in the residue was determined as 14% by glc (10% FFAP; 180°).

Reaction of Phenylboron Dichloride with Ethyl Diazoacetate  
at -25°.

To a solution of phenylboron dichloride (3.18 g; 20 mmole) in ether (25 ml) was slowly added a solution of



ethyl diazoacetate (4.38 g; 38.5 mmole) at -25°. Nitrogen evolution, measured by an azotometer, was rapid but smooth. Cooling the reaction mixture below -40° caused the separation of an oil from the solution. The addition was completed at -25° and after 1.5 hr the nitrogen evolution was 92% (based on diazo compound). The reaction mixture was worked up as above and analysis of the residue by glc (10% FFAP; 180°) showed the presence of 21% of ethyl phenylacetate.

Reaction of Phenylboron Dichloride with Ethyl Diazoacetate in THF.

To a solution of phenylboron dichloride (1.59 g; 10 mmole) in THF (30 ml) was slowly added a solution of ethyl diazoacetate (2.19 g; 19 mmole) at -52°. Monitoring of gas evolution with an azotometer showed no reaction at this temperature. However, upon warming to -27° the evolution of nitrogen commenced and was slow and smooth. After 2.25 hr 86% of theory (based on diazo ester) had been evolved. The reaction was worked up as described above and the yield of ethyl phenylacetate in the residue was determined as 100% by glc. The residue was subjected to distillation at reduced pressure and afforded 1.64 g (98%) ethyl phenylacetate, bp 84-85° (3 mm) (lit <sup>117</sup> bp 120-1 (20 mm))  $n_D^{23.5} = 1.4992$ . ir (liquid film) 1730 (ester C=O), 1490, 1450 720  $\text{cm}^{-1}$  ( $\text{C}_6\text{H}_5$ ): nmr  $\tau$ : 2.63 (s, 5)



$C_6H_5^-$ , 5.81 (q,2)  $OCH_2CH_3$ , 6.39 (s,2)  $C_6H_5CH_2$ , 8.78 (t,3)  $CH_3CH_2O$ ; mass spectrum  $m/e$ : 164(38), 92(26), 91(100), 65(28), 49(13), 29(41).

Reaction of Phenylboron Dichloride with Diazoacetophenone.

To a solution of phenylboron dichloride (1.59 g; 10 mmole) in THF (30 ml) was slowly added a solution of diazo-acetophenone (2.04 g; 14 mmole) in THF (25 ml) at -20°. Nitrogen evolution was monitored with an azotometer but at this temperature was found to be negligible. Consequently the reaction mixture was warmed to -14°. Nitrogen evolution was slow but smooth and after 2 hr was quantitative. The reaction mixture was worked up as described above and the yield of deoxybenzoin in the residue was determined as 35% by glc (10% FFAP; 200°). A sample of the product was isolated by preparative thin layer chromatography (silica gel, elution with 1:1 benzene:pentane). ir ( $CHCl_3$ ) 3000-3100, 1590, 1490, 1450, 700 ( $C_6H_5$ ),  $1690\text{ cm}^{-1}$  (C=O); nmr  $\tau$ : 1.90 - 2.80 (m, 10p)  $C_6H_5 \times 2$ , 5.78 (s,2)  $CH_2C\ddot{O}$ .



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